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L1 30 (PNA AND (ANTISENSE (W) AGENT#))/BI,AB

=> d l1 bib ab

L1 ANSWER 1 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:631234 CAPLUS
TI Hybridization of complementary and homologous peptide nucleic acid probes to folded DNA targets
AU Armitage, Bruce A.; Kushon, Stuart A.; Datta, Bhaskar; Schmitt, Christoph; Jordan, Jason P.
CS Department of Chemistry, Carnegie Mellon University, Pittsburgh, PA, 15213-3890, USA
SO Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003 (2003), COMP-074 Publisher: American Chemical Society, Washington, D. C. CODEN: 69EKY9
DT Conference; Meeting Abstract
LA English
AB Folding of natural DNA and RNA sequences imposes thermodn. barriers to hybridization by ***antisense*** ***agents*** . This lecture will focus on the thermodn. of hybridization in two model folded structures: a DNA hairpin and a DNA quadruplex. The hairpin forms when two complementary sequences are sepd. by a short noncomplementary region. DNA quadruplexes can

arise from folding of guanine-rich sequences. The basic unit of the quadruplex is a guanine tetrad, in which four guanines are simultaneously hydrogen bonded into a square array. Stacking of G-tetrads is facilitated by cation binding. Complementary peptide nucleic acid (***PNA***) probes were synthesized to target these structures and the thermodn. of hybridization were measured using temp.-dependent UV absorbance expts. In addn., a quadruplex-forming DNA was targeted using a homologous, rather than complementary, ***PNA*** probe. The ***PNA*** successfully recognized the G-rich DNA and formed a hybrid PNA2-DNA2 quadruplex, representing the first demonstration of homologous hybridization.

=> d l1 2-30 bib ab

L1 ANSWER 2 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:432117 CAPLUS
TI Targeting of folded nucleic acids with complementary and homologous ***PNA*** hybridization probes
AU Armitage, Bruce A.
CS Department of Chemistry, Mellon College of Science, Carnegie Mellon University, Pittsburgh, PA, USA
SO Abstracts, 31st Northeast Regional Meeting of the American Chemical Society, Saratoga Springs, NY, United States, June 15-18 (2003), 45 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69EBFV
DT Conference; Meeting Abstract
LA English
AB The antisense strategy for regulating gene expression is well established in the lab. and one antisense drug has reached the clinic. This approach involves hybridization between the ***antisense*** ***agent*** and its complementary sequence within the target RNA. A potential complication in this approach is restricted access of the ***antisense*** ***agent*** to its target sequence due to folding of the RNA. Aside from the kinetic implications of RNA folding on hybridization, thermodn. penalties will be incurred due to the energetic cost of unfolding the RNA in order to access the target sequence. This lecture will focus on the thermodn. of hybridization in two model folded structures: a DNA hairpin and a DNA quadruplex. The hairpin forms when two complementary sequences are sepd. by a short noncomplementary region. DNA quadruplexes can arise from folding of guanine-rich sequences. The basic unit of the quadruplex is a guanine tetrad, in which four guanines are simultaneously hydrogen bonded into a square array. Stacking of G-tetrads is facilitated by cation binding. Complementary peptide nucleic acid (***PNA***) probes were synthesized to target these structures and the thermodn. of hybridization were measured using temp.-dependent UV absorbance expts. In addn., a quadruplex-forming DNA was targeted using a homologous, rather than complementary, ***PNA*** probe. The ***PNA*** successfully recognized the G-rich DNA and formed a hybrid PNA2-DNA2 quadruplex, representing the first demonstration of homologous hybridization.

L1 ANSWER 3 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:805617 CAPLUS
DN 139:64923
TI (2'-O-methyl-RNA)-3'- ***PNA*** chimeras: A new class of mixed backbone oligonucleotide analogues with high binding affinity to RNA
AU Greiner, Beate; Breipohl, Gerhard; Uhlmann, Eugen
CS Aventis Pharma Deutschland GmbH, Frankfurt a.M., D-65926, Germany
SO Helvetica Chimica Acta (2002), 85(9), 2619-2626
CODEN: HCACAV; ISSN: 0018-019X
PB Verlag Helvetica Chimica Acta
DT Journal
LA English
OS CASREACT 139:64923
AB The automated online synthesis of DNA-3'- ***PNA*** chimeras 1-4 and (2'-O-methyl-RNA)-3'- ***PNA*** chimeras 5-8 is described, in which the 3'-terminal part of the oligonucleotide is linked to the N-terminal part of the ***PNA*** via N-(.omega.-hydroxyalkyl)-N-[(thymin-1- yl)acetyl]glycine units (alkyl=Et, Ph, Bu, and pentyl). By means of UV thermal denaturation, the binding affinities of all chimeras were directly compared by detg. their Tm values in the duplex with complementary DNA and RNA. All investigated DNA-3'- ***PNA*** chimeras and (2'-O-methyl-RNA)-3'- ***PNA*** chimeras form more-stable duplexes with complementary DNA and RNA than the corresponding unmodified DNA. Interestingly, a N-(3-hydroxypropyl)glycine linker resulted in the highest binding affinity for DNA-3'- ***PNA*** chimeras, whereas the (2'-O-methyl-RNA)-3'- ***PNA*** chimeras showed optimal binding with the homologous N-(4-hydroxybutyl)glycine linker. The duplexes of (2'-O-methyl-RNA)-3'- ***PNA*** chimeras and RNA were significantly more stable than those contg. the corresponding DNA-3'- ***PNA*** chimeras. Surprisingly, we found that the charged (2'-O-methyl-RNA)-3'- ***PNA*** chimera with a N-(4-hydroxybutyl)glycine-based unit at the junction to the ***PNA*** part shows the same binding affinity to RNA as uncharged ***PNA*** . Potential applications of (2'-O-methyl-RNA)-3'- ***PNA*** chimeras include their use as ***antisense*** ***agents*** acting by a RNase-independent mechanism of action, a prerequisite for antisense-oligonucleotide-mediated correction of aberrant splicing of pre-mRNA.
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 4 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:692218 CAPLUS
DN 138:118081
TI Lipid-mediated introduction of peptide nucleic acids into cells
AU Braasch, Dwaine A.; Corey, David R.
CS Department of Pharmacology and Biochemistry, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, USA

SO Methods in Molecular Biology (Totowa, NJ, United States) (2002), 208(Peptide Nucleic Acids), 211-223 CODEN: MMBIED; ISSN: 1064-3745
PB Humana Press Inc.
DT Journal
LA English
AB Peptide oligonucleotides have been used as ***antisense*** ***agent*** to block gene expression or to alter RNA splicing. This report describes a method for the delivery of peptide nucleic acids (PNAs) into cells as ***PNA*** -DNA heteroduplexes complexed with cationic lipid.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 5 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:586341 CAPLUS
DN 138:299849
TI Imaging gene expression in the brain in vivo in a transgenic mouse model of Huntington's disease with an antisense radiopharmaceutical and drug-targeting technology
AU Lee, Hwa Jeong; Boado, Ruben J.; Braasch, Dwaine A.; Corey, David R.; Pardridge, William M.
CS Department of Medicine, UCLA School of Medicine, Los Angeles, CA, USA
SO Journal of Nuclear Medicine (2002), 43(7), 948-956 CODEN: JNMEAQ; ISSN: 0161-5505
PB Society of Nuclear Medicine
DT Journal
LA English
AB Disease-specific genes of unknown function can be imaged in vivo with antisense radiopharmaceuticals, providing the transcellular, transport of these mols. is enabled with drug-targeting technol. The current studies describe the prodn. of 16-mer peptide nucleic acid (***PNA***) that is antisense around the methionine initiation codon of the huntingtin gene of Huntington's disease (HD). Methods: The ***PNA*** is biotinylated, which allows for rapid capture by a conjugate of streptavidin and the rat 8D3 monoclonal antibody (mAb) to the mouse transferrin receptor (TfR), and contains a tyrosine residue, which enables radiolabeling with 125I. The reformulated ***PNA*** antisense radiopharmaceutical that is conjugated to the 8D3 mAb is designated 125I- ***PNA*** /8D3. This form of the ***PNA*** is able to access endogenous transferrin transport pathways at both the blood-brain barrier and the brain cell membrane and undergoes both import from the blood to the brain and export from the brain to the blood through the TfR. Results: The ability of the ***PNA*** to hybridize to the target huntingtin RNA, despite conjugation to the mAb, was shown both with cell-free translation assays and with RNase protection assays. The 125I- ***PNA*** /8D3 conjugate was administered i.v. to either littermate control mice or to R6/2 transgenic mice, which express the exon 1 of the human HD gene. The mice were sacrificed 6 h later for frozen sectioning of the brain and quant. autoradiog. The studies showed a 3-fold increase in sequestration of the 125I- ***PNA*** /8D3 antisense radiopharmaceutical in the brains of the HD transgenic mice in vivo, consistent with the selective expression of the HD exon-1 mRNA in these animals. Conclusion: These results support the hypothesis that gene expression in vivo can be quantitated with antisense radiopharmaceuticals, providing these mols. are reformulated with drug-targeting technol. Drug targeting enables access of the ***antisense*** ***agent*** to endogenous transport pathways, which permits passage across the cellular barriers that sep. blood and intracellular compartments of target tissues.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 6 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:529814 CAPLUS
DN 137:346791
TI Peptide nucleic acids targeted to the mouse proNPFFA reveal an endogenous opioid tonus
AU Bonnard, Elisabeth; Mazarguil, Honore; Zajac, Jean-Marie
CS CNRS UMR 5089, Institut de Pharmacologie et de Biologie Structurale, Toulouse, 31077, Fr.
SO Peptides (New York, NY, United States) (2002), 23(6), 1107-1113 CODEN: PPTDD5; ISSN: 0196-9781
PB Elsevier Science Inc.
DT Journal
LA English
AB Pharmacol. studies have implicated the anti-opioid neuropeptide FF (NPFF) in the modulation of pain transmission. Since its physiol. role has not yet been fully elucidated, the present study examd. whether antisense peptide nucleic acid (***PNA***) complementary to the NPFF precursor (proNPFFA) modified pain sensitivity. Mice received three i.p. injections (10 mg/kg) of antisense ***PNA*** (As-proNPFFA) over a period of 24 h. As-proNPFFA treatment significantly increased the basal tail withdrawal latency in the tail-flick test. This analgesia persisted during 2 days and was completely reversed by naloxone. Thus, antisense PNAs, by decreasing anti-opioid effects, revealed a basal endogenous opioid activity. Our results evidence a physiol. interplay between NPFF and opioid systems and further support the use of ***PNA*** as effective ***antisense*** ***agents*** , for studying gene function in vivo.
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 7 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:424605 CAPLUS
DN 137:159196
TI Inhibition of Macrophage iNOS by Selective Targeting of Antisense ***PNA***
AU Chiarantini, Laura; Cerasi, Aurora; Fraternale, Alessandra; Andreoni, Francesca; Scari, Sonia; Giovine, Marco; Clavarino, Emanuela; Magnani, Mauro
CS Institute of Biochemistry "Giorgio Fornaini", Universita degli Studi di Urbino, Italy
SO Biochemistry (2002), 41(26), 8471-8477 CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal

LA English
AB Peptide nucleic acids (PNAs) are synthetic polynucleobases that bind to DNA and RNA with high affinity and specificity and with poor membrane permeability. Although PNAs have an enormous potential as ***antisense*** ***agents*** , the success of antisense ***PNA*** applications will require efficient cellular uptake. In this study, a unique antisense 14-mer anti-inducible nitric oxide synthase (iNOS) was encapsulated into erythrocytes (RBC) by hypotonic dialysis. RBC loaded with ***PNA*** (10.5 .+. 3.5 .mu.mol/mL RBC) were targeted specifically to murine macrophages, taking advantage of an in vitro opsonization induced by ZnCl2 and bis-sulfosuccynimidil-suberate (BS3). This in vitro opsonization enhanced the phagocytosis of loaded RBC and the delivery of ***PNA*** into macrophages (0.72 pmol/106 macrophages). The efficacy of this delivery system is demonstrated by decreases in NO prodn. and iNOS protein expression inside the macrophage. Therefore, we can suggest this novel approach for biomedical application.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 8 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:209592 CAPLUS
DN 137:89853
TI Cell permeabilization and uptake of antisense peptide-peptide nucleic acid (***PNA***) into Escherichia coli
AU Eriksson, Magdalena; Nielsen, Peter E.; Good, Liam
CS Department of Physical Chemistry, Chalmers University of Technology, Goeteborg, SE-41296, Swed.
SO Journal of Biological Chemistry (2002), 277(9), 7144-7147 CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Peptide nucleic acid (***PNA***) is a DNA mimic with promising properties for the development of ***antisense*** ***agents*** . Antisense PNAs targeted to Escherichia coli genes can specifically inhibit gene expression, and attachment of ***PNA*** to the cell-permeabilizing peptide KFFKFFKFFK dramatically improves antisense potency. The improved potency obsd. earlier was suggested to be due to better cell uptake; however, the uptake kinetics of std. or modified PNAs into bacteria had not been investigated. Here we monitored outer and inner membrane permeabilization by using chem. probes that normally are excluded from cells but can gain access at points where membrane integrity is disturbed. Membrane permeabilization was much more rapid in the presence of peptide- ***PNA*** conjugates relative to the free components used alone or in combination. Indeed, peptide-PNAs permeabilized E. coli nearly as quickly as antimicrobial peptides. Furthermore, as expected for outer membrane-active compds., added MgCl2 reduced cell-permeabilization. Concurrent monitoring of outer and inner membrane permeabilization indicated that passage across the outer membrane is rate-limiting for uptake. The enhanced cell-permeation properties of peptide-PNAs can explain their potent antisense activity, and the results indicate an unanticipated synergy between the peptide and ***PNA*** components.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 9 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:46836 CAPLUS
DN 137:79206
TI Novel ***antisense*** ***agents*** based on peptide nucleic acids (PNAs)
AU Verheijen, Jeroen C.; van der Marel, Gijs A.; van Boom, Jacques H.
CS Leiden Institute of Chemistry, Gorlaeus Laboratories, Leiden, 2300 RA, Neth.
SO Innovation and Perspectives in Solid Phase Synthesis & Combinatorial Libraries: Peptides, Proteins and Nucleic Acids--Small Molecule Organic Chemistry Diversity, Collected Papers, International Symposium, 6th, York, United Kingdom, Aug. 31-Sept. 4, 1999 (2001), Meeting Date 1999, 145-148. Editor(s): Epton, Roger. Publisher: Mayflower Scientific Ltd., Kingswinford, UK. CODEN: 69CEGV; ISBN: 0-9515735-3-5
DT Conference
LA English
AB A symposium report. The solid phase synthesis of two novel classes of ***PNA*** based ***antisense*** ***agents*** with the ability to destroy the target RNA strand is described. The ribonucleolytic activity could be bestowed on ***PNA*** by the covalent attachment of the 5'-phosphorylated-2',5'-linked oligoadenylate (2-5A) to yield a 2-5A- ***PNA*** hybrid.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 10 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:815867 CAPLUS
DN 136:128433
TI Targeting of cancer-related proteins with ***PNA*** oligomers
AU Pooga, Margus; Langel, Ulo
CS Estonian Biocentre, Tartu, EE-51010, Estonia
SO Current Cancer Drug Targets (2001), 1(3), 231-239 CODEN: CCDTB9; ISSN: 1568-0096
PB Bentham Science Publishers Ltd.
DT Journal; General Review
LA English
AB A review. Aberrant gene expression is characteristic to all cancer cells and pathophysiol. in general. Selective inhibition of constitutively elevated expression of oncogenes provides an opportunity to hinder the proliferation of malignant cells. Small synthetic mols. that specifically interfere with transcription and/or translation have great potential as anticancer drugs. Currently first-generation antisense oligonucleotides are widely used to inhibit the oncogene expression. The second generation of ***antisense*** ***agents*** have been studied

mainly in vitro. One of these agents, peptide nucleic acid (***PNA***) is an oligonucleotide mimic with a noncharged achiral polyamide backbone to which the nucleobases are linked. ***PNA*** oligomers bind tightly to complementary DNA or RNA and are very stable in biol. fluids. ***PNA*** can inhibit transcription and translation of target genes by specifically hybridizing to DNA or mRNA. The in vitro expts. showing inhibition of target protein expression by ***PNA*** have been followed by the first successful applications of ***PNA*** as an ***antisense*** ***agent*** in cultured cells and also in vivo. Hopefully this will lead to a wider use of ***PNA*** in the studies of cancer biol. and therapy.
RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 11 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:749715 CAPLUS
DN 136:16848
TI Effect of Secondary Structure on the Thermodynamics and Kinetics of ***PNA*** Hybridization to DNA Hairpins
AU Kushon, Stuart A.; Jordan, Jason P.; Seifert, Jennifer L.; Nielsen, Henrik; Nielsen, Peter E.; Armitage, Bruce A.
CS Department of Chemistry, Carnegie Mellon University, Pittsburgh, PA, 15213-3890, USA
SO Journal of the American Chemical Society (2001), 123(44), 10805-10813 CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB The binding of a series of ***PNA*** and DNA probes to a group of unusually stable DNA hairpins of the tetraloop motif has been obsd. using absorbance hypochromicity (ABS), CD (CD), and a colorimetric assay for ***PNA*** /DNA duplex detection. These results indicate that both stable ***PNA*** -DNA and DNA-DNA duplexes can be formed with these target hairpins, even when the melting temps. for the resulting duplexes are up to 50 .degree.C lower than that of the hairpin target. Both hairpin/single-stranded and hairpin/hairpin interactions are considered in the scope of these studies. Secondary structures in both target and probe mols. are shown to depress the melting temps. and free energies of the probe-target duplexes. Kinetic anal. of hybridization yields reaction rates that are up to 160-fold slower than hybridization between two unstructured strands. The thermodn. and kinetic obstacles to hybridization imposed by both target and probe secondary structure are significant concerns for the continued development of ***antisense*** ***agents*** and esp. diagnostic probes.
RE.CNT 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 12 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:435821 CAPLUS
DN 135:206946
TI ***PNA*** oligomers as tools for specific modulation of gene expression
AU Pooga, Margus; Land, Tiit; Bartfai, Tamas; Langel, Ulo
CS Department of Neurochemistry and Neurotoxicology, Arrhenius Laboratories, Stockholm University, Stockholm, S-10691, Swed.
SO Biomolecular Engineering (2001), 17(6), 183-192 CODEN: BIENFV; ISSN: 1389-0344
PB Elsevier Science B.V.
DT Journal; General Review
LA English
AB A review with 67 refs. Small synthetic mols. that can specifically inhibit translation and/or transcription have shown great promise as potential antisense/antigene drugs. Peptide nucleic acid (***PNA***), an oligonucleotide mimic, has a non-charged achiral polyamide backbone to which the nucleobases are attached. ***PNA*** oligomers are extremely stable in biol. fluids and they specifically hybridize to DNA or RNA in a complementary manner, forming very strong heteroduplexes. Some of the mRNAs have yet undetd. and possibly long half-lives, successful down regulation of gene expression by antisense oligonucleotides (ON) requires that the ***antisense*** ***agent*** is long lived. ***PNA*** fulfils this requirement better than phosphodiester or phsphorothioate ONs. ***PNA*** can inhibit transcription and translation of resp. genes by tight binding to DNA or mRNA. First in vitro expts. to specifically down regulate protein expression by ***PNA*** have been followed by successful antisense and antigene application of ***PNA*** oligomers in vivo. This review discusses the principles of the in vitro and in vivo use of ***PNA*** oligonucleotides.
RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 13 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:48033 CAPLUS
DN 134:290359
TI A short phosphodiester window is sufficient to direct RNase H-dependent RNA cleavage by antisense peptide nucleic acid
AU Malchere, Charlotte; Verheijen, Jeroen; Van Der Laan, Sander; Bastide, Lionel; Van Boom, Jacques; Lebleu, Bernard; Robbins, Ian
CS Institut de Genetique Moleculaire, UMR 5535 and EP 2030, CNRS, Montpellier, F-34293, Fr.
SO Antisense & Nucleic Acid Drug Development (2000), 10(6), 463-468 CODEN: ANADF5; ISSN: 1087-2906
PB Mary Ann Liebert, Inc.
DT Journal
LA English
AB The potential pharmacol. benefits of using peptide nucleic acid (***PNA***) as an ***antisense*** ***agent*** are tempered by its incapacity to activate RNase H. The mixed backbone oligonucleotide (ON) (or gapmer) approach, in which a short internal window of RNAse H-competent residues is embedded within an RNase H-incompetent ON has not been applied previously to ***PNA*** because ***PNA*** and DNA hybridize to RNA with

very different helical structures, creating structural perturbations at the two ***PNA*** -DNA junctions. It is demonstrated here for the first time that a short internal phosphodiester window within a ***PNA*** is sufficient to evoke the RNase H-dependent cleavage of a targeted RNA and to abrogate translation elongation in a well-characterized in vitro assay.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 14 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:15936 CAPLUS
DN 134:193678
TI Peptide conjugates of oligonucleotides as enhanced ***antisense*** ***agents***
AU Stetsenko, D. A.; Arzumanov, A. A.; Korshun, V. A.; Gait, M. J.
CS Laboratory of Molecular Biology, Medical Research Council, Cambridge, CB2 2QH, UK
SO Molecular Biology (Translation of Molekulyarnaya Biologiya (Moscow)) (2000), 34(6), 852-859 CODEN: MOLBBJ; ISSN: 0026-8933
PB MAIK Nauka/Interperiodica Publishing
DT Journal; General Review
LA English
AB A review with eighty-two refs. The use of synthetic oligonucleotides and their analogs to block gene expression by binding the complementary RNA sequences in cells, the antisense principle, has been limited by poor uptake of the agents by cells in culture. This review describes attempts to harness by chem. conjugation the ability of certain peptides that may cross membranes to enhance the cellular uptake of oligonucleotides. These include fusogenic and hydrophobic peptides, nuclear localization signals, receptor targeting and translocating peptides, and various combinations. We also outline briefly some popular methods of peptide-oligonucleotide conjugation. Finally, we review the use of noncovalent peptide additives and the recent studies of conjugates of peptide nucleic acid (***PNA***) with peptides.
RE.CNT 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 15 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:868956 CAPLUS
DN 135:176118
TI Inhibition of neomycin phosphorotransferase expression in Entamoeba histolytica with antisense peptide nucleic acid (***PNA***) oligomers
AU Stock, Roberto P.; Olvera, Alejandro; Scarfi, Sonia; Sanchez, Ricardo; Ramos, Marco A.; Boffa, Lidia C.; Benatti, Umberto; Landt, Olfert; Alagon, Alejandro
CS Instituto de Biotecnologia, Universidad Nacional Autonoma de Mexico (UNAM), Morelos, 62210, Mex.
SO Archives of Medical Research (2000), 31(4, Suppl.), S271-S272 CODEN: AEDEER; ISSN: 0188-4409
PB Elsevier Science Inc.
DT Journal
LA English
AB ***PNA*** oligomers were used as ***antisense*** ***agents*** for down-regulation of the bacterial gene for neomycin phosphotransferase (NPT) in E. histolytica in culture. The antisense ***PNA*** inhibited NPT activity by 70%; the scrambled control ***PNA*** oligomer did not have a significant effect. This study suggests that ***PNA*** oligomers may provide a valuable tool for genetic studies in E. histolytica and may be feasible gene-therapeutic agents against amebiasis.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 16 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:866533 CAPLUS
DN 134:111186
TI Inhibition of Gene Expression Inside Cells by Peptide Nucleic Acids: Effect of mRNA Target Sequence, Mismatched Bases, and ***PNA*** Length
AU Doyle, Donald F.; Braasch, Dwaine A.; Simmons, Carla G.; Janowski, Bethany A.; Corey, David R.
CS Departments of Pharmacology and Biochemistry, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, 75390-9041, USA
SO Biochemistry (2001), 40(1), 53-64 CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB Genome sequencing has revealed thousands of novel genes, placing renewed emphasis on chem. approaches for controlling gene expression. Antisense oligomers designed directly from the information generated by sequencing are one option for achieving this control. Here we explore the rules governing the inhibition of gene expression by peptide nucleic acids (PNAs) inside cells. PNAs are a DNA/RNA mimic in which the phosphate deoxyribose backbone has been replaced by uncharged linkages. Binding to complementary sequences is not hindered by electrostatic repulsion and is characterized by high rates of assocn. and elevated affinities. Here we test the hypothesis that the favorable properties of PNAs offer advantages for recognition of mRNA and antisense inhibition of gene expression in vivo. We have targeted 27 PNAs to 18 different sites throughout the 5'-untranslated region (5'-UTR), start site, and coding regions of luciferase mRNA. PNAs were introduced into living cells in culture as ***PNA*** -DNA-lipid complexes, providing a convenient high throughput method for cellular delivery. We find that PNAs targeted to the terminus of the 5'-UTR are potent and sequence-specific ***antisense*** ***agents*** . PNAs fifteen to eighteen bases in length were optimal inhibitors. The introduction of one or two mismatches abolished inhibition, and complementary PNAs targeted to the sense strand were also inactive. In striking contrast to effective inhibition by PNAs directed to the terminal region, PNAs complementary to other sites within the 5'-UTR do not inhibit gene expression. We also observe no inhibition by PNAs complementary to the start site or rest of the coding region, nor do we detect inhibition by PNAs that are highly C/G rich and possess extremely high affinities for their target

sequences. Our results suggest that PNAs can block binding of the translation machinery but are less able to block the progress of the ribosome along mRNA. The high specificity of antisense inhibition by PNAs emphasizes both the promise and the challenges for PNAs as ***antisense*** ***agents*** and provides general guidelines for using PNAs to probe the mol. recognition of biol. targets inside cells.
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 17 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:223282 CAPLUS
DN 133:145595
TI Antisense inhibition of .delta.-opioid receptor gene function in vivo by peptide nucleic acids
AU Fraser, Graeme L.; Holmgren, Janna; Clarke, Paul B. S.; Wahlestedt, Claes
CS AstraZeneca R and D, Montreal, QC, Can.
SO Molecular Pharmacology (2000), 57(4), 725-731 CODEN: MOPMA3; ISSN: 0026-895X
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Peptide nucleic acids (***PNA***) are synthetic analogs of DNA that hybridize to complementary oligonucleotide sequences with exceptional affinity and target specificity. The stability of ***PNA*** in biol. fluids together with the unique hybridization characteristics of these structures suggests that ***PNA*** may have considerable potential as ***antisense*** ***agents*** for exptl. use in vivo. To test this hypothesis, we attempted to modulate supraspinal .delta.-opioid receptor function in rats using ***PNA*** sequences designed to be complementary to a region of the rat .delta.-opioid receptor. Repeated i.c.v. administration of ***PNA*** over a period of 5 days significantly inhibited the antinociceptive response and locomotor response to selective .delta.-opioid receptor agonists. ***PNA*** attenuated .delta.-opioid receptor function in a sequence-specific, target-specific, and reversible manner characteristic of the functional inhibition caused by an antisense mechanism. There were no apparent toxicities arising from the ***PNA*** treatment based on the behavior of the animals and inspection of the treated tissues. Satn. binding studies on brain homogenates did not reveal any significant difference in receptor Bmax between treatment groups. However, [35S]guanosine-5'-O-(3-thio)triphosphate binding assays demonstrated a significant decrease in agonist efficacy in homogenates prepd. from antisense-treated rats. Taken together, these results demonstrate that peptide nucleic acids are effective ***antisense*** ***agents*** in vivo and suggest that ***PNA*** may be a useful alternative to phosphodiester or phosphorothioate oligonucleotides, or variants thereof, for detn. of gene function in vivo.
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 18 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:760681 CAPLUS
DN 132:160707
TI Antisense properties of peptide nucleic acid
AU Larsen, H. J.; Bentin, T.; Nielsen, P. E.
CS Biochemistry Laboratory B, Department of Medical Biochemistry and Genetics, Center for Biomolecular Recognition, The Panum Institute, University of Copenhagen, Copenhagen, DK-2200, Den.
SO Biochimica et Biophysica Acta (1999), 1489(1), 159-166 CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier Science B.V.
DT Journal; General Review
LA English
AB A review with 48 refs. Peptide nucleic acid (***PNA***) is a nucleic acid mimic in which the deoxyribose phosphate backbone has been replaced by a pseudo-peptide polymer to which the nucleobases are linked. ***PNA*** -oligomers can be synthesized in relatively large amts., are highly stable in biol. environments, and bind complementary DNA and RNA targets with remarkably high affinity and specificity. Thus ***PNA*** possesses many of the properties desired for a good ***antisense*** ***agent*** . Until recently, limited uptake of ***PNA*** into cells has been the major obstacle for applying ***PNA*** as an ***antisense*** ***agent*** in cell cultures and in vivo. Here, the antisense properties of ***PNA*** in vitro and in vivo will be reviewed. In particular, we will focus on recent observations indicating that ***PNA*** equipped with or without various uptake moieties may function as an efficient and gene-specific inhibitor of translation in Escherichia coli and in certain mammalian cell types.
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 19 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:501533 CAPLUS
DN 132:194633
TI ***PNA*** /DNA chimeras
AU Uhlmann, Eugen; Greiner, Beate; Breipohl, Gerhard
CS Hoechst Marion Roussel Deutschland GmbH Chemical Research G 838, Frankfurt am Main, D-65926, Germany
SO Peptide Nucleic Acids (1999), 51-70. Editor(s): Nielsen, Peter E.; Egholm, Michael. Publisher: Horizon Scientific Press, Norfolk, UK. CODEN: 67YLA6
DT Conference
LA English
AB A convenient method for the solid-support synthesis of ***PNA*** /DNA chimeras is described which makes use of monomethoxytrityl/acyl-protected monomeric building blocks. The acid-labile monomethoxytrityl (Mmt) group is employed for the temporary protection of the amino function of aminoethyl-glycine, while the exocyclic amino functions of the nucleobases are protected with ammonia-cleavable acyl protecting groups. This orthogonal protecting-group strategy is fully compatible with the std. phosphoramidite DNA synthesis method. The resulting ***PNA*** /DNA

chimeras obey the Watson-Crick rules on binding to complementary DNA and RNA. Binding affinity of the ***PNA*** -DNA chimeras strongly depends on the ***PNA*** :DNA ratio. The ***PNA*** /DNA chimeras bind with higher affinity to RNA than to DNA, and the type of linking moiety between ***PNA*** and DNA could be adjusted to obtain optimal binding affinity. In addn. to their promising binding properties, ***PNA*** -DNA chimeras can also assume biol. functions, such as a primer function for DNA polymerases. Pure PNAs cannot induce RNase H cleavage of target RNA, which often supports the biol. efficacy of ***antisense*** ***agents*** . In contrast, the DNA- ***PNA*** chimeras are able to stimulate cleavage of the target RNA by RNase H on formation of a RNA chimera duplex.
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 20 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:91165 CAPLUS
TI Minimal modification of antisense oligonucleotides
AU Uhlmann, E.
CS Chemical Research, Hoechst Marion Roussel, Frankfurt, 65926, Germany
SO Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), CARB-005
Publisher: American Chemical Society, Washington, D. C. CODEN: 67GHA6
DT Conference; Meeting Abstract
LA English
AB Uniformly phosphorothioate (PS) modified oligodeoxynucleotides (ODN) are ***antisense*** ***agents*** of the first generation. Although a no. of PS-ODN are in advanced stages of clin. development and the first antisense drug (Vitravene; Isis Pharmaceuticals) has been approved by the FDA, certain limitations of PS-ODN have emerged. Our approach to overcome these limitations is to reduce the no. of PS linkages within the ODN to a min. which is necessary to stabilize against nucleotlytic degrdn. We have developed a novel protection strategy which is a combination of the end-capping technique and the PS protection of internal pyrimidine positions which are the major sites of endonuclease degrdn. This protection scheme has successfully been used for specific inhibition of expression of various genes. Advantageously, it can also be combined with secondary modifications at the carbohydrate moieties, such as 2'-O-alkyl-modifications, or with partial replacement of the sugar phosphate backbone by 2-aminoethylglycine-based ***PNA*** units (peptide nucleic acid) leading to DNA- ***PNA*** chimeras.

L1 ANSWER 21 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:618936 CAPLUS
DN 129:227036
TI Peptide nucleic acids (***PNA***) and ***PNA*** -DNA chimeras. From high binding affinity towards biological function
AU Uhlmann, Eugen
CS Hoechst Marion Roussel Deutschland G.m.b.H., Frankfurt/Main, D-65926, Germany
SO Biological Chemistry (1998), 379(8/9), 1045-1052
CODEN: BICHF3; ISSN: 1431-6730
PB Walter de Gruyter & Co.
DT Journal; General Review
LA English
AB A review is given with 45 refs. Oligonucleotide analogs are of major interest as tools in mol. biol., as diagnostics, and as potential pharmaceuticals which bind in a predictable way to certain nucleic acid target sequences, aiming at the inhibition of expression of disease-causing genes. One of the most promising nucleic acid mimetics are the peptide- or polyamide- nucleic acids (***PNA***) which bind with higher affinity to DNA and RNA than natural oligonucleotides. In these non-ionic PNAs, the entire sugar-phosphate backbone is replaced by an N-amino-ethylglycine-based polyamide structure. A unique property of ***PNA*** is its ability to displace one strand of a DNA double-helix. This strand displacement process, which is inefficient with DNA, is supported by the formation of an unusually stable internal (***PNA***), DNA triple helix. The combination of ***PNA*** and DNA in 1 mol. results in ***PNA*** /DNA chimeras with new properties. They show improved aq. soly. compared to pure PNAs due to their partially neg. charged structure. The cellular uptake of the chimeras is better than of pure PNAs. In contrast to ***PNA*** , the chimeras bind exclusively in the antiparallel orientation under physiol. conditions. The binding affinity is generally stronger when the ***PNA*** /DNA chimeras are hybridized to RNA than to DNA, whereby the strength of binding strongly depends on the ***PNA*** : DNA ratio. ***PNA*** /DNA chimeras are recognized as substrates by various nucleic acid processing enzymes, and consequently can also assume biol. functions, such as a primer function for DNA polymerases. Pure ***PNA*** cannot induce RNase H cleavage of target RNA, which is believed to support the biol. efficacy of ***antisense*** ***agents*** . DNA- ***PNA*** chimeras are able to stimulate cleavage of the target RNA by RNase H upon formation of an RNA chimera duplex.

L1 ANSWER 22 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:240564 CAPLUS
DN 129:2614
TI Antisense inhibition of gene expression in bacteria by ***PNA*** targeted to mRNA
AU Good, Liam; Nielsen, Peter E.
CS Center for Biomolecular Recognition, IMBG, Department of Biochemistry, Panum Inst., Univ. of Copenhagen, Copenhagen, Den.
SO Nature Biotechnology (1998), 16(4), 355-358
CODEN: NABIF9; ISSN: 1087-0156
PB Nature America
DT Journal
LA English
AB Peptide nucleic acid (***PNA***) is a DNA mimic with attractive properties for developing improved gene-targeted ***antisense*** ***agents*** . To test this potential of ***PNA*** in bacteria, PNAs were designed to target the start codon regions of the Escherichia coli .beta.-galactosidase and .beta.-lactamase genes. Dose-dependent and specific gene inhibition was obsd. in vitro using low nanomolar

PNA concns. and in vivo using low micromolar concns. Inhibition was more efficient for a permeable E. coli strain relative to wild-type K-12. The potency of the anti-.beta.-lactamase PNAs was abolished by a six base substitution, and inhibition could be re-established using a ***PNA*** with compensating base changes. Antisense inhibition of the .beta.-lactamase gene was sufficient to sensitize resistant cells to the antibiotic ampicillin. The results demonstrate gene- and sequence-specific antisense inhibition in E. coli and open possibilities for antisense antibacterial drugs and gene function analyses in bacteria.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 23 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:30501 CAPLUS
DN 128:115214
TI Synthesis of oligo(5-aminopentanoic acid)-nucleobases (APN): potential ***antisense*** ***agents***
AU Bergmeier, Stephen C.; Fundy, Susan L.
CS Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, The Ohio State University, Columbus, OH, 43210-1291, USA
SO Bioorganic & Medicinal Chemistry Letters (1997), 7(24), 3135-3138 CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Oligomers of 5-aminopentanoic acid nucleobases have been prepd. for use an ***antisense*** ***agents*** . The synthesis of the 5'-end starter unit and the 3'-end monomer unit, as well as the coupling procedures used for oligomer formation are described. For example, the trimeric 5-aminopentanoate-based nucleobase I (Cbz = PhCH2OCO; Boc = Me3COCO) was prepd. in 51% yield using the starting materials of NH(CH2CH2OH)2, 2-oxopiperidine and N3-benzoylthymine.
RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 24 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:433595 CAPLUS
DN 127:95571
TI Synthesis and Characterization of a Peptide Nucleic Acid Conjugated to a D-Peptide Analog of Insulin-like Growth Factor 1 for Increased Cellular Uptake
AU Basu, Soumitra; Wickstrom, Eric
CS Department of Microbiology and Immunology and Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA, 19107, USA
SO Bioconjugate Chemistry (1997), 8(4), 481-488 CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
AB DNA therapeutics show great potential for gene-specific, nontoxic therapy of a wide variety of diseases. The deoxyribose phosphate backbone of DNA has been modified in a no. of ways to improve nuclease stability and cell membrane permeability. Recently, a new DNA deriv. with an amide backbone instead of a deoxyribose phosphate backbone, peptide nucleic acid (***PNA***), has shown tremendous potential as an ***antisense*** ***agent*** . Although PNAs hybridize very strongly and specifically to RNA and DNA, they are taken up by cells very poorly, limiting their potential as nucleic acid binding agents. To improve cellular uptake of a ***PNA*** sequence, it was conjugated to a D-amino acid analog of insulin-like growth factor 1 (IGF1), which binds selectively to the cell surface receptor for insulin-like growth factor 1 (IGF1R). The IGF1 D-peptide analog was assembled on (4-methylbenzhydryl)amine resin, and then the ***PNA*** was extended as a continuation of the peptide. The conjugate and control sequences were radiolabeled with 14C or fluorescently labeled with fluorescein isothiocyanate. Cellular uptake of the ***PNA*** -peptide conjugate, a control with two alanines in the peptide, and a control ***PNA*** without the peptide segment were studied in murine BALB/c 3T3 cells, which express low levels of murine IGF1R, in p6 cells, which are BALB/c 3T3 cells which overexpress a transfected human IGF1R gene, and in human Jurkat cells, which do not express IGF1R, as a neg. control. The specific ***PNA*** -peptide conjugate displayed much higher uptake than the control ***PNA*** , but only in cells expressing IGF1R. This approach may allow cell-specific and tissue-specific application of PNAs as gene-regulating agents in vivo.

L1 ANSWER 25 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:13375 CAPLUS
DN 126:114098
TI Specific and nonspecific inhibition of transcription by DNA, ***PNA*** , and phosphorothioate promoter analog duplexes
AU Hamilton, Susan E.; Iyer, Mridula; Norton, James C.; Corey, David R.
CS Southwest. Med. Cent., Univ. Texas, Dallas, TX, 75235, USA
SO Bioorganic & Medicinal Chemistry Letters (1996), 6(23), 2897-2900 CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier
DT Journal
LA English
AB DNA duplexes analogous to the promoters for SP6 or T7 RNA polymerase inhibit transcription with exquisite selectivity. By contrast, phosphorothioate oligomers inhibit nonselectively, and peptide nucleic acid (***PNA***) duplexes and ***PNA*** :DNA heteroduplexes do not inhibit at all. The absence of recognition of proteins by PNAs may prove to be a substantial advantage for their use as ***antisense*** ***agents*** and nucleic acid probes.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 26 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:108346 CAPLUS
DN 124:282134

TI Antisense properties of duplex- and triplex-forming PNAs
AU Knudsen, Helle; Nielsen, Peter E.
CS Department Medical Biochemistry Genetics, Panum Institute, Copenhagen, DK-2200, Den.
SO Nucleic Acids Research (1996), 24(3), 494-500 CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB The potential of peptide nucleic acids (PNAs) as specific inhibitors of translation was studied. PNAs with a mixed purine/pyrimidine sequence form duplexes, whereas homopyrimidine PNAs form (***PNA***)2/RNA triplexes with complementary sequences on RNA. Neither of these ***PNA*** /RNA structures are substrates for RNase H. Translation expts. performed in cell-free exts. showed that a 15mer duplex-forming RNA blocked translation in a dose-dependent manner when the target was 5'-proximal to the AUG start codon on the RNA, whereas similar 10-, 15- or 20mer PNAs had no effect when targeted towards sequences in the coding region. Triplex-forming 10mer PNAs were efficient and specific ***antisense*** ***agents*** with a target overlapping the AUG start codon and caused arrest of ribosome elongation with a target positioned in the coding region of the mRNA. Furthermore, translation could be blocked with a 6mer bisPNA or with a clamp ***PNA*** , forming partly a triplex, partly a duplex, with its target sequence in the coding region of the mRNA.

L1 ANSWER 27 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:563178 CAPLUS
DN 123:189662
TI An assessment of the antisense properties of RNase H-competent and steric-blocking oligomers
AU Bonham, Michele A.; Brown, Stephen; Boyd, Ann L.; Brown, Pamela H.; Bruckenstein, David A.; Hanvey, Jeffery C.; Thomson, Stephen A.; Pipe, Adrian; Hassman, Fred; et al.
CS Dep. Mol. Cell Biol., Glaxo Res. Inst., Research Triangle Park, NC, 27709, USA
SO Nucleic Acids Research (1995), 23(7), 1197-203 CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB The antisense activity and gene specificity of two classes of oligonucleotides (ONs) were directly compared in a highly controlled assay. One class of ONs has been proposed to act by targeting the degrdn. of specific RNAs through an RNase H-mediated mechanism and consists of C-5 propynyl pyrimidine phosphorothioates ONs (propyne-S-ON). The second class of ***antisense*** ***agents*** has been proposed to function by sterically blocking target RNA formation, transport or translation and includes sugar modified (2'-O-allyl) ONs and peptide nucleic acids (PNAs). Using a CV-1 cell based microinjection assay, the authors targeted ***antisense*** ***agents*** representing both classes to various cloned sequences localized within the SV40 large T antigen RNA. The authors detd. the propyne-S-ON was the most potent and gene-specific agent of the two classes which likely reflected its ability to allow RNase H cleavage of its target. The ***PNA*** oligomer inhibited T Ag expression via an antisense mechanism, but was less effective than the propyne-S-ON; the lack of potency may have been due in part to the PNAs slow kinetics of RNA assocn. Interestingly, unlike the 2'-O-allyl ON, the antisense activity of the ***PNA*** was not restricted to the 5' untranslated region of the T Ag RNA. Based on these findings the authors conclude that PNAs could be effective ***antisense*** ***agents*** with addnl. chem. modification that will lead to more rapid assocn. with their RNA target.

L1 ANSWER 28 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:362885 CAPLUS
DN 122:214508
TI Positive-ion fast-atom bombardment tandem mass spectrometry of peptide nucleic acids
AU Takao, Toshifumi; Fukuda, Hiroyuki; Coull, James; Shimonishi, Yasutsugu
CS Inst. Protein Res., Osaka Univ., Osaka, 565, Japan
SO Rapid Communications in Mass Spectrometry (1994), 8(12), 925-8 CODEN: RCMSEF; ISSN: 0951-4198
PB Wiley
DT Journal
LA English
AB The base sequence of synthetic peptide nucleic acids (PNAs), novel ***antisense*** ***agents*** , was analyzed by pos.-ion fast-atom bombardment tandem mass spectrometry (FAB-MS/MS). Upon high-energy collisional activation decompn., ***PNA*** oligomers provided apparent MS/MS product ions resulting from specific cleavage along the ***PNA*** backbone.

L1 ANSWER 29 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:621881 CAPLUS
DN 121:221881
TI NMR solution structure of a peptide nucleic acid complexed with RNA
AU Brown, Stephen C.; Thomson, Stephen A.; Veal, James M.; Davis, Donald G.
CS Glaxo Res. Inst., Res. Triangle Park, NC, 27709, USA
SO Science (Washington, DC, United States) (1994), 265(5173), 777-7 CODEN: SCIEAS; ISSN: 0036-8075
DT Journal
LA English
AB Peptide nucleic acids (***PNA***) incorporating nucleic acid bases into an achiral polyamide backbone bind to DNA in a sequence-dependent manner. The structure of a ***PNA*** -RNA complex was detd. with NMR methods. A hexameric ***PNA*** formed a 1:1 complex with a complementary RNA that is an antiparallel, right-handed double helix with Watson-Crick base pairing similar to the "A" form structure of RNA duplexes. The achiral ***PNA*** backbone assumed a distinct conformation upon binding that differed from previously proposed models and provides a basis for further structure-based design of ***antisense*** ***agents*** .

L1 ANSWER 30 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:124252 CAPLUS
DN 120:124252
TI Characterization of antisense binding properties of peptide nucleic acids by capillary gel electrophoresis
AU Rose, Donald J.
CS Bioanal. Struct. Chem. Dep., Glaxo Res. Inst., Research Triangle Park, NC, 27709, USA
SO Analytical Chemistry (1993), 65(24), 3545-9
CODEN: ANCHAM; ISSN: 0003-2700
DT Journal
LA English
AB The binding of peptide nucleic acids (PNAs), novel ***antisense*** ***agents*** , to their complementary oligonucleotide is characterized by capillary gel electrophoresis (CGE). The ability of CGE to resolve the free and bound species enables the measurement of relative binding kinetics and the stoichiometry of binding. The binding kinetics depend on the relative sequence orientation of the target oligonucleotides. The stoichiometry of binding is 1:1 for the ***PNA*** -oligodeoxynucleotide heteroduplex whereas the stoichiometry for the ***PNA*** -oligoribonucleotide is more complicated.

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=> caplus
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FULL ESTIMATED COST 0.21 0.21

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FILE LAST UPDATED: 21 Dec 2003 (20031221/ED)
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=> s cook, philip/au
L1 3 COOK, PHILIP/AU

=> e cook, p/au
E1 3 COOK Y/AU
E2 1 COOK YVONNE/AU
E3 0 --> COOK, P/AU
E4 1 COOKAND D R/AU
E5 37 COOKE A/AU
E6 2 COOKE A C/AU
E7 1 COOKE A D A/AU
E8 2 COOKE A F/AU
E9 62 COOKE A H/AU
E10 5 COOKE A I/AU
E11 8 COOKE A J/AU
E12 1 COOKE A J D/AU

=> e cook/au
E1 10 COOIL BRUCE J/AU
E2 1 COOIL BRUCE K/AU
E3 3 --> COOK/AU
E4 45 COOK A/AU
E5 14 COOK A A/AU
E6 1 COOK A B/AU
E7 1 COOK A BRAMWELL/AU
E8 33 COOK A C/AU
E9 1 COOK A D/AU
E10 2 COOK A E/AU
E11 13 COOK A F/AU
E12 2 COOK A F II/AU

=> e cook p/au
E1 2 COOK OSCAR A/AU
E2 2 COOK OTTO W/AU
E3 21 --> COOK P/AU
E4 13 COOK P A/AU
E5 2 COOK P B/AU
E6 6 COOK P C/AU
E7 24 COOK P D/AU
E8 125 COOK P DAN/AU
E9 5 COOK P E/AU

E10 12 COOK P F/AU
E11 1 COOK P F E/AU
E12 20 COOK P G/AU

=> s e3 or e8 21 "COOK P"/AU 125 "COOK P DAN"/AU
L2 146 "COOK P"/AU OR "COOK P DAN"/AU

=> s (pna or peptide(w)nucleic(w)acid)/bi,ab 5002 PNA/BI 4737 PNA/AB 301846 PEPTIDE/BI 220888 PEPTIDE/AB 149948 NUCLEIC/BI 65160 NUCLEIC/AB 3758424 ACID/BI 2487398 ACID/AB 1386 PEPTIDE(W)NUCLEIC(W)ACID
L3 5344 (PNA OR PEPTIDE(W)NUCLEIC(W)ACID)/BI,AB

=> s l2 an dl3
MISSING OPERATOR L2 AN
The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> s l2 and l3
L4 0 L2 AND L3

=> s (antisense or anti(w)sense)/bi,ab 32591 ANTISENSE/BI 22877 ANTISENSE/AB 319946 ANTI/BI 256454 ANTI/AB 31358 SENSE/BI 30001 SENSE/AB 1132 ANTI(W)SENSE
L5 33290 (ANTISENSE OR ANTI(W)SENSE)/BI,AB

=> s l3 and l4
L6 0 L3 AND L4

=> d his
(FILE 'HOME' ENTERED AT 13:54:11 ON 22 DEC 2003)
FILE 'CAPLUS' ENTERED AT 13:54:20 ON 22 DEC 2003
L1 3 S COOK, PHILIP/AU E COOK, P/AU E COOK/AU E COOK P/AU
L2 146 S E3 OR E8
L3 5344 S (PNA OR PEPTIDE(W)NUCLEIC(W)ACID)/BI,AB
L4 0 S L2 AND L3
L5 33290 S (ANTISENSE OR ANTI(W)SENSE)/BI,AB
L6 0 S L3 AND L4

=> s l2 and l5
L7 51 L2 AND L5

=> s l2 and l3
L8 0 L2 AND L3

=> s l3 and l5

L9 291 L3 AND L5

=> s l7 and l9
L10 0 L7 AND L9

=> d his
(FILE 'HOME' ENTERED AT 13:54:11 ON 22 DEC 2003)
FILE 'CAPLUS' ENTERED AT 13:54:20 ON 22 DEC 2003
L1 3 S COOK, PHILIP/AU E COOK, P/AU E COOK/AU E COOK P/AU
L2 146 S E3 OR E8
L3 5344 S (PNA OR PEPTIDE(W)NUCLEIC(W)ACID)/BI,AB
L4 0 S L2 AND L3
L5 33290 S (ANTISENSE OR ANTI(W)SENSE)/BI,AB
L6 0 S L3 AND L4
L7 51 S L2 AND L5
L8 0 S L2 AND L3

L9 291 S L3 AND L5

L10 0 S L7 AND L9

=> d l9 1-291 bib ab

L9 ANSWER 1 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:986624 CAPLUS
TI Cyclic ***PNA*** -based compound directed against HIV-1 TAR RNA: modelling, liquid-phase synthesis and TAR binding
AU Depecker, Geoffrey; Patino, Nadia; Di Giorgio, Christophe; Terreux, Raphael; Cabrol-Bass, Daniel; Bailly, Christian; Aubertin, Anne-Marie; Condom, Roger
CS Laboratoire de Chimie Bioorganique, UMR UNSA-CNRS 6001, Faculte des Sciences, Universite de Nice-Sophia Antipolis, Fr.
SO Organic & Biomolecular Chemistry (2003), 2(1), 74-79
CODEN: OBCRAK; ISSN: 1477-0520
PB Royal Society of Chemistry
DT Journal
LA English
AB A cyclic mol. including a hexameric ***PNA*** sequence has been designed and synthesized in order to target the TAR RNA loop of HIV-1 through the formation of a "kissing complex". For comparison, its linear analog has also been investigated. The synthesis of the cyclic and linear ***PNA*** has been accomplished following a liq.-phase strategy using mixed ***PNA*** and fully N-protected (aminoethylglycinamide) fragments. The interactions of this cyclic ***PNA*** and its linear analog with TAR RNA have been studied and the results indicate clearly that no interaction occurs between the cyclic ***antisense*** ***PNA*** and TAR RNA, whereas a tenuous interaction has been detected with its linear ***PNA*** analog.

L9 ANSWER 2 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:950458 CAPLUS
TI Nucleic acid and corresponding protein 121P1F1 useful in treatment and detection of human cancer
IN Challita-Eid, Pia M.; Hubert, Rene S.; Raitano, Arthur B.; Faris, Mary; Afar, Daniel E. H.; Ge, Wangmao; Jakobovits, Aya
PA USA
SO U.S. Pat. Appl. Publ., 211 pp., Cont.-in-part of U.S. Ser. No. 779,250. CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- --------------- --------
PI US 2003223997 A1 20031204 US 2002-87190 20020228 US 2001015159 A1 20010823 US 2001-779250 20010208 US 6481360 B2 20021119
PRAI US 2001-779250 A2 20010208 US 1999-388322 A3 19990901
AB A novel gene (designated 121P1F1) and its encoded protein, and variants thereof, are described wherein 121P1F1 exhibits tissue specific expression in normal adult tissue, and is aberrantly over-expressed in the cancers of the prostate, bladder, kidney, colon, lung, and pancreas. Northern blot expression anal. shows a restricted expression pattern in adult tissues. Consequently, 121P1F1 provides a diagnostic, prognostic, prophylactic, and/or therapeutic target for cancer. The 121P1F1 gene or fragment thereof, or its encoded protein, or variants thereof, or a fragment thereof, can be used to elicit a humoral or cellular immune response; antibodies or T cells reactive with 121P1F1 can be used in active or passive immunization.

L9 ANSWER 3 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:939065 CAPLUS
TI A Targeted ***Peptide*** ***Nucleic*** ***Acid*** To Down-Regulate Mouse Microsomal Triglyceride Transfer Protein Expression in Hepatocytes

AU van Rossenberg, Sabine M. W.; Sliedregt-Bol, Karen M.; Prince, Perry; van Berkel, Theo J. C.; van Boom, Jacques H.; van der Marel, Gijs A.; Biessen, Erik A. L.
CS Leiden/Amsterdam Center for Drug Research, Division of Biopharmaceutics and Leiden Institute of Chemistry, Gorlaeus Laboratories, Leiden University, Leiden, 2300, Neth.
SO Bioconjugate Chemistry (2003), 14(6), 1077-1082 CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
AB Peptide nucleic acids (***PNA*** 's) have shown to hold potential as ***antisense*** drugs. In this study we have designed ***PNA*** drugs for the microsomal triglyceride transfer protein (MTP), which is known to play a crit. role in the assembly of atherogenic lipoproteins, and have converted the most potent drug into a liver-targeted prodrug. First, we have synthesized three ***PNA*** sequences targeting domains on the mouse MTP mRNA, which were not involved in intrastrand base-pairing interactions as jugded from its secondary structure. Only one of the ***PNA*** 's, PNA569, showed dose-dependent inhibition of MTP expression in a cell-free system for coupled transcription/translation of MTP. Second, to improve the cellular uptake of this ***PNA*** drug, we have conjugated PNA569 to a high affinity ligand for the asialoglycoprotein receptor, K(GalNAc)2. As compared to the parent ***PNA*** , the prodrug ***PNA*** -K(GalNAc)2 was found to display to a markedly improved capacity to inhibit MTP mRNA expression in parenchymal liver cells. A glycoconjugated nonsense control appeared to be ineffective. In conclusion, the design of a targeted ***PNA*** is described to reduce MTP expression in parenchymal liver cells by 70%. The presented approach for targeted tissue-specific down-regulation of genes by ***PNA*** 's may be valid for other genes as well.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:938737 CAPLUS
TI Synthetic developments towards ***PNA*** -peptide conjugates
AU de Koning, Martijn C.; van der Marel, Gijs A.; Overhand, Mark
CS Leiden Institute of Chemistry, Leiden University, PO Box 9502, Leiden, 2300 RA, Neth.
SO Current Opinion in Chemical Biology (2003), 7(6), 734-740 CODEN: COCBF4; ISSN: 1367-5931
PB Elsevier Science Ltd.
DT Journal
LA English
AB Since the discovery of peptide nucleic acids (PNAs) as DNA mimics in the early 1990s, a tremendous effort has been directed to their application as ***antisense*** and antigene probes. With the aim of further enhancing their properties, PNAs have been conjugated to a variety of effector mols. Among these, small peptide fragments, often derived from functional proteins, are able to convey their specific properties to the conjugate.

L9 ANSWER 5 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:924429 CAPLUS
TI Blockade of plasmid replication mediated by peptide nucleic acids
AU Liebling, Michael R.; Jou, Nainn-tsyr; Fang, Wayne; Louie, James S.
CS Beijing, Peop. Rep. China
SO Molecular Biotechnology (2003), 25(3), 229-240 CODEN: MLBOEO; ISSN: 1073-6085
PB Humana Press Inc.
DT Journal
LA English
AB Because peptide nucleic acids (PNAs) are capable of blocking amplification of DNA (DNA) by Taq DNA polymerase in vitro, we postulated that PNAs might be able to block replication in vivo. To explore this possibility, we assessed the ability of ***PNA*** to specifically block the replication of pUC19 plasmids by allowing a ***PNA*** , directed against segments of the Ampr sequence to bind to pUC19 prior to electroporation into Escherichia coli, strain DH10B. Colonies produced by this maneuver not only remained sensitive to ampicillin but were also incapable of blue color prodn. on X-gal-contg. media, thus demonstrating true blockade of pUC19 replication, rather than ***antisense*** activity. The ability of the ***PNA*** to prevent pUC19 replication in these expts. was shown to be dose related. Attempts to prevent the replication of E. coli using a ***PNA*** directed against a portion of the lac Z sequence found within the bacterial genome were not uniformly successful. Subsequent expts. showed that the electroporated ***PNA*** did not consistently enter a sufficient no. of cells for an effect to be demonstrated in the assays used. Nonetheless, this is the first demonstration of in vivo complete replication blockade by a ***PNA*** and opens up the potential for new forms of specific antibiosis in both prokaryotic and eukaryotic cells.

L9 ANSWER 6 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:892908 CAPLUS
DN 139:369676
TI Composition of endosomolytic spermine and methods for delivery of nucleic acids
IN Satishchandran, C.
PA Nucleonics, Inc., USA
SO PCT Int. Appl., 98 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2003093449 A2 20031113 WO 2003-US14288 20030506
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2002-378191P P 20020506
AB This invention features methods and compns. for delivery of nucleic acids (e.g., DNA, RNA, ***PNA*** , and hybrids thereof) to cells. Specifically, the compn. includes a nucleic acid, an endosomolytic spermine that includes a cholesterol or fatty acid, and a targeting spermine that includes a ligand for a cell surface mol. The nucleic acid delivery complexes of the invention permit biol. active nucleic acids to be delivered to cells and organisms in vitro and in vivo in a manner and form that allows the nucleic acids to carry out their desired biol. function.

L9 ANSWER 7 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:892646 CAPLUS
DN 139:381754
TI Synthesis of transporter oligopeptide- ***PNA*** conjugates for use in transmembrane treatment of disease or infection
IN Tolborg, Jakob; Frandsen, Torben Peter; Nielsen, Bjarne Ronfeldt; Johansen, Charlotte; Kjaerulff, Soren

PA Pantheco A/S, Den.
SO PCT Int. Appl., 96 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2003092736 A2 20031113 WO 2003-DK280 20030501 W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI DK 2002-661 A 20020501
AB The present invention relates to ***peptide*** ***nucleic*** ***acid*** (***PNA***) conjugates TP-L- ***PNA*** [(I); TP = transporter peptide; L = linker group; ***PNA*** = ***peptide*** ***nucleic*** ***acid*** 4 - 35mer], to methods for their prepn., to compns. comprising the conjugates and to the use of these conjugates as medicaments and their use in therapy (no data), e.g. in the treatment of infections, and further concerns cell penetrating peptides and methods of conjugating the peptides with ***PNA*** (no data). Thus I (TP = H-KFFKFFKFFK; L = .beta.-Ala-.beta.-cyclohexyl-L-Ala; ***PNA*** = TTCAAACATAGT-NH2) was prepd. using solid-phase synthetic techniques. To study transporter peptide effectiveness, 30 L-oligopeptides and 2 D-oligopeptides were used in in vitro studies of Rifampicin transport against E. coli, P. aeruginosa, K. pneumoniae, and E. faecium species. All but one proposed transporter oligopeptide showed a decrease in Min. Inhibitory Concn. of Rifampicin against one or more tested bacteria.

L9 ANSWER 8 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:891640 CAPLUS
TI Antibiotic-free bacterial strain selection using ***antisense*** ***peptide*** ***nucleic*** ***acid***
AU Dryselius, Rikard; Nekhotiaeva, Natalia; Nielsen, Peter E.; Good, Liam
CS Karolinska Institutet, Stockholm, Swed.
SO BioTechniques (2003), 35(5), 1060-1062,1064 CODEN: BTNQDO; ISSN: 0736-6205
PB Eaton Publishing Co.
DT Journal
LA English
AB Antibiotics are widely useful in medicine, agriculture, and industrial fermns. However, increasing problems with resistant strains call for restrained use and alternative strategies. ***Antisense*** peptide nucleic acids (PNAs) show potent bactericidal effects when targeted against the essential Escherichia coli acpP gene. Aside from attractive antimicrobial therapeutic possibilities for such ***antisense*** PNAs, we considered that they could be used as a substitute for antibiotics in bacterial strain selection. Here, treatment of a mixt. of E. coli wild-type cells and cells carrying a binding-site altered copy of acpP (acpP-1) with anti-acpP ***PNA*** completely killed wild-type cells within 2 h, whereas cells carrying acpP-1 proliferated. Furthermore, electrotransformation of E. coli cells with the plasmid carrying acpP-1 followed by ***PNA*** selection gave rise to only true transformants. Unlike previous antibiotic-free selection strategies, this procedure does not require special growth environments or special host strains. Also, the ***PNA*** -selected cells grow at a near normal rate. The results open possibilities to use ***antisense*** PNAs for strain selection and construction in research and industrial application.
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:874217 CAPLUS
TI ***Antisense*** ***peptide*** ***nucleic*** ***acid*** -mediated knockdown of the p75 neurotrophin receptor delays motor neuron disease in mutant SOD1 transgenic mice
AU Turner, Bradley J.; Cheah, Irwin K.; MacFarlane, Katherine J.; Lopes, Elizabeth C.; Petratos, Steven; Langford, Steven J.; Cheema, Surindar S.
CS Howard Florey Institute of Experimental Physiology and Medicine, University of Melbourne, Australia
SO Journal of Neurochemistry (2003), 87(3), 752-763 CODEN: JONRA9; ISSN: 0022-3042
PB Blackwell Publishing Ltd.
DT Journal
LA English
AB Re-expression of the death-signalling p75 neurotrophin receptor (p75NTR) is assocd. with injury and neurodegeneration in the adult nervous system. The induction of p75NTR expression in mature degenerating spinal motor neurons of humans and transgenic mice with amyotrophic lateral sclerosis (ALS) suggests a role of p75NTR in the progression of motor neuron disease (MND). In this study, we designed, synthesized and evaluated novel ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***) constructs targeting p75NTR as a potential gene knockdown therapeutic strategy for ALS. An 11-mer ***antisense*** ***PNA*** directed at the initiation codon, but not downstream gene sequences, dose-dependently inhibited p75NTR expression and death-signalling by nerve growth factor (NGF) in Schwann cell cultures. ***Antisense*** phosphorothioate oligonucleotide (PS-ODN) sequences used for comparison failed to confer such inhibitory activity. Systemic i.p. administration of this ***antisense*** ***PNA*** to mutant superoxide dismutase 1 (SOD1G93A) transgenic mice significantly delayed locomotor impairment and mortality compared with mice injected with nonsense or scrambled ***PNA*** sequences. Redns. in p75NTR expression and subsequent caspase-3 activation in spinal cords were consistent with increased survival in ***antisense*** ***PNA*** -treated mice. The uptake of fluorescent-labeled ***antisense*** ***PNA*** in the nervous system of transgenic mice was also confirmed. This study suggests that p75NTR may be a promising ***antisense*** target in the treatment of ALS.
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:837243 CAPLUS
DN 139:333100
TI Methods for targeting quadruplex DNA conformation used for diagnosis and treatment of colorectal cancer
IN Siddiqui-Jain, Adam; Grand, Cory L.; Bearss, David J.; Hurley, Laurence H.; Farrell, Thomas J.
PA Cyternex, Inc., USA; The Arizona Board of Regents On Behalf of the University of Arizona
SO PCT Int. Appl., 69 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2003087317 A2 20031023 WO 2003-US10658 20030404 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE,

GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2002-370358P P 20020405 US 2002-404966P P 20020820 US 2003-456637P P 20030320
AB This invention presents methods for targeting quadruplex DNA conformation used for diagnosis and treatment of colorectal cancer. Among the different intrastrand quadruplex structures that can arise from duplex DNA, it has been discovered that a chair conformation is biol. significant. Also, it has been detd. that certain mutations in quadruplex forming nucleotide sequences destabilize quadruplex structure and are assocd. with cancer. In this invention, quadruplex formation is demonstrated using sequences from the genes c-myc, ret, pdgfA, pdgfB, and vegf. Methods of prodn. and use of destabilized quadruplex nucleic acids for colorectal cancer diagnostics and prognostics, as well as ***antisense*** nucleic acid cancer therapies, are provided. Also addressed in this invention are methods for identifying compds. that modulate the biol. activity of a native quadruplex DNA in a chair conformation, such as TMPyP2 and TMPyP4.

L9 ANSWER 11 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:829485 CAPLUS
TI Synthesis of Radiometal-Labeled and Fluorescent Cell-Permeating Peptide- ***PNA*** Conjugates for Targeting the bcl-2 Proto-oncogene
AU Gallazzi, Fabio; Wang, Yi; Jia, Fang; Shenoy, Nalini; Landon, Linda A.; Hannink, Mark; Lever, Susan Z.; Lewis, Michael R.
CS Molecular Biology Program, Department of Veterinary Medicine and Surgery, Department of Chemistry, Department of Biochemistry, University of Missouri- Columbia, Columbia, MO, 65211, USA
SO Bioconjugate Chemistry (2003), 14(6), 1083-1095 CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
AB The B-cell lymphoma/leukemia-2 (bcl-2) proto-oncogene has been assocd. with the transformation of benign lesions to malignancy, disease progression, poor prognosis, reduced survival, and development of resistance to radiation and chemotherapy in many types of cancer. The objective of this work was to synthesize an ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***) complementary to the first six codons of the bcl-2 open reading frame, conjugated to a membrane-permeating peptide for intracellular delivery, and modified with a bifunctional chelating agent for targeting imaging and therapeutic radiometals to tumors overexpressing bcl-2. Four peptide- ***PNA*** constructs were synthesized by a combination of manual and automated stepwise elongation techniques, including bcl-2 ***antisense*** conjugates and nonsense conjugates with no complementarity to any known mammalian gene or DNA sequence. The ***PNA*** sequences were synthesized manually by solid-phase 9-fluorenylmethoxycarbonyl (Fmoc) techniques. Then a fully protected lysine monomer, modified with 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''- tetraacetic acid (DOTA) for radiometal chelation, was coupled manually to each ***PNA*** sequence. Synthesis of the DOTA- ***PNA*** conjugates was followed by automated elongation with a peptide sequence (PTD-4-glycine, PTD-4-G), known to mediate cellular internalization of impermeable effector mols., or its retro-inverso analog (ri-PTD-4-G). Prepn. of the four conjugates required an innovative synthetic strategy, using mild acid conditions to generate hydrophobic, partially deprotected intermediates. These intermediates were purified by semipreparative reversed-phase HPLC and completely deprotected to yield pure peptide- ***PNA*** conjugates in 6% to 9% overall yield. Using modifications of this synthetic strategy, the ri-PTD-4-G conjugate of bcl-2 ***antisense*** ***PNA*** was prepd. using a lysine deriv. of tetramethylrhodamine (TMR) for fluorescence microscopy. Plasma stability studies showed that 111In-DOTA-labeled ri-PTD-4-G-anti-bcl-2 ***PNA*** was stable for 168 h at 37 .degree.C, unlike the conjugate contg. the parent peptide sequence. Scanning confocal fluorescence microscopy of TMR-labeled ri-PTD-4-G-anti-bcl-2 ***PNA*** in Raji lymphoma cells demonstrated that the retro-inverso peptide was active in membrane permeation and mediated cellular internalization of the ***antisense*** ***PNA*** into the cytoplasm, where high concns. of bcl-2 mRNA are expected to be present.
RE.CNT 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:805079 CAPLUS
DN 139:316203
TI Gene therapy for arterial proliferative diseases and progressive renal diseases by nucleic acid medicines
AU Fukuda, Noboru
CS Second Dep. Intern. Med., Nihon Univ. Sch. Med., Japan
SO Nichidai Igaku Zasshi (2003), 62(7), 329-336 CODEN: NICHAS; ISSN: 0029-0424
PB Nihon Daigaku Igakkai
DT Journal; General Review
LA Japanese
AB A review. Nucleic acid medicines such as ***antisense*** DNA, ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***), ribozyme, and decoy are expected to be novel therapeutic strategy for severe diseases which are resistant to present therapy. We have developed ***antisense*** DNA, ***antisense*** ***PNA*** and ribozyme targeting platelet-derived growth factor (PDGF) A-chain and transforming growth factor (TGF)-.beta.1 for arterial proliferative diseases such as coronary artery stenosis after angioplasty or stent implantation, hypertensive vascular diseases and atherosclerosis, and progressive renal diseases. ***Antisense*** DNA to PDGF A-chain inhibited arterial growth in spontaneously hypertensive rats without lowering blood pressure and inhibited the neointima formation of pig coronary artery after stent implantation. Ribozymes to PDGF A-chain and TGF-.beta.1 specifically inhibited the target transcripts and prevented the neointima formation. Ribozymes to TGF-.beta.1 improved renal damages in hypertensive rats. These nucleic acid medicines targeting PDGF A-chain and TGF-.beta.1 will be feasible gene therapies for the arterial proliferative diseases and progressive renal diseases. Pyrrole-imidazole polyamides are novel gene therapy compd., which bind to minor grove of double strand DNA by base-specific manner to inhibit gene expression. We developed pyrrole-imidazole polyamide to TGF-.beta.1 and found that the polyamide binds to the TGF-.beta.1 promoter. The polyamide significantly inhibited TGF-.beta.1 promoter activity and decreased expression of TGF-.beta.1 mRNA and protein. Pyrrole-imidazole polyamide administered perorally was obviously uptaken in vascular and renal tissues in rats in vivo, suggesting that the pyrrole-imidazole polyamide will be a peroral gene therapy agent.

L9 ANSWER 13 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:778230 CAPLUS
TI Radiolabeled PNAs for imaging gene expression

AU Wickstrom, Eric; Sauter, Edward; Tian, Xianben; Rao, Sampath; Quin, Weyng; Thakur, Mathew
CS Thomas Jefferson University, Philadelphia, PA, 19107, USA
SO Brazilian Archives of Biology and Technology (2002), 45(Spec. Issue), 57-59 CODEN: BABTFC; ISSN: 1516-8913
PB Instituto de Tecnologia do Parana
DT Journal
LA English
AB Scintigraphic imaging of gene expression in vivo by non-invasive means could precisely direct physicians to appropriate intervention at the onset of disease and could contribute extensively to the management of patients. However no method is currently available to image specific overexpressed oncogene mRNAs in vivo by scintigraphic imaging. Nevertheless, we have obsd. that Tc-99m-peptides can delineate tumors, and that ***PNA*** -peptides are specific for receptors on malignant cells and are taken up specifically and concd. in nuclei. We hypothesize that ***antisense*** Tc-99m- ***PNA*** -peptides will be taken up by human breast cancer cells, hybridize to complementary mRNA targets, and permit imaging of oncogene mRNAs in human breast cancer xenografts in a mouse model, providing a proof-of-principle for non-invasive detection of precancerous and invasive breast cancer. Oncogenes cyclin D1, erbB-2, c-MYC, and tumor suppressor p53 will be probed. If successful, this technique will be useful for diagnostic imaging of other solid tumors as well.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:759207 CAPLUS
TI ***Peptide*** ***nucleic*** ***acid*** and its application in biology
AU Bao, Shixiang; Hua, Ling; Huang, Huiqin
CS National Key Biotechnology Laboratory for Tropical Crops, CATAS, Haikou, Hainan Province, 571101, Peop. Rep. China
SO Zhongguo Shenghua Yaowu Zazhi (2002), 23(5), 263-265 CODEN: ZSYZFP; ISSN: 1005-1678
PB Zhongguo Shenghua Yaowu Zazhi Bianjibu
DT Journal; General Review
LA Chinese
AB Peptide nucleic acids (PNAs) are electroneutral, synthetic DNA analogs, resistant to the degrdn. by by nuclease or protease, and can bind to DNA or RNA to form di- or tri-helix structure. It can be applied in gene diagnosis of diseases, development of ***antisense*** pharmaceuticals, gene expression and regulation, gene sequence and structure anal., as well as in life origin.

L9 ANSWER 15 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:714479 CAPLUS
TI Inhibition of Gene Expression by Peptide Nucleic Acids in Cultured Cells
AU Cogoi, Susanna; Rapozzi, Valentina; Xodo, Luigi E.
CS Department of Biochemical Sciences and Technologies, Udine, 33100, Italy
SO Nucleosides, Nucleotides & Nucleic Acids (2003), 22(5-8), 1615-1618 CODEN: NNNAFY; ISSN: 1525-7770
PB Marcel Dekker, Inc.
DT Journal
LA English
AB We have tested in cultured cells the capacity of ***antisense*** and antigene PNAs to inhibit, in a sequence specific manner, the expression of oncogenes in leukemia and pancreatic carcinoma cells. The results obsd. appeared promising and suggest that ***PNA*** may play in the future an important role in targeting disease-related genes.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 16 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:714478 CAPLUS
TI Covalent Coupling of a PIM-1 Oncogene Targeted ***PNA*** with an Antennapedia Derived Peptide
AU Bertrand, J.-R.; Sumbatyan, N.; Malvy, C.
CS CNRS, Institut Gustave Roussy, Villejuif, UMR 8121, Fr.
SO Nucleosides, Nucleotides & Nucleic Acids (2003), 22(5-8), 1611-1613 CODEN: NNNAFY; ISSN: 1525-7770
PB Marcel Dekker, Inc.
DT Journal
LA English
AB Peptide nucleic acids (***PNA***) are promising ***antisense*** mol. for blocking gene expression in cell culture or in vivo. Nevertheless because they are poor efficient to pass the cellular membrane, it is necessary to use a vectorisation agent to observe an inhibitory effect. We describe the coupling of the rhodamine labeled 17-mer ***antisense*** ***PNA*** to a fusogenic peptide from antenapedia via S-S linkage, the studies of the penetration of this complex into fibroblast cells and its inhibitory effect on piml targeted protononcogene.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:714234 CAPLUS
TI Phosphono Peptide Nucleic Acids with a Constrained Hydroxyproline-Based Backbone
AU Efimov, Vladimir A.; Klykov, Valeryi N.; Chakhmakhcheva, Oksana G.
CS Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Moscow, 117997, Russia
SO Nucleosides, Nucleotides & Nucleic Acids (2003), 22(5-8), 593-599 CODEN: NNNAFY; ISSN: 1525-7770
PB Marcel Dekker, Inc.
DT Journal
LA English
AB DNA mimics representing neg. charged analogs of peptide nucleic acids (PNAs), particularly hetero-oligomers constructed from alternating phosphono- ***PNA*** residues (pPNA) and monomers on the base of trans-4-hydroxy-L-proline (HypNA) as well as mimics composed of phosphono-HypNA monomers (pHypNA) were tested in a set of in vitro and in vivo assays, and they demonstrated a high potential for the use in nucleic acid based diagnostic, isolation of nucleic acids and ***antisense*** expts.
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 18 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:697035 CAPLUS
DN 139:224969
TI Nucleic acid and polypeptide sequences for sperm protein enkurin and uses thereof for contraception and fertility treatment
IN Florman, Harvey; Jungnickel, Melissa; Sutton, Keith
PA University of Massachusetts, USA
SO PCT Int. Appl., 106 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2003072749 A2 20030904 WO 2003-US5920 20030225
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,

LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2002-359870P P 20020225
AB The invention claims polynucleotide and polypeptide sequences for a protein, enkurin, that is preferentially expressed in human and mouse sperm. The invention also claims sequences for calcium channel TRPC2, protein isoform TRPC2-S, and RNA splicing variants. Enkurin binds to TRPCs (Transient Receptor Potential Classics) including TRPC2-S, a protein encoded by TRPC2 that is not predicted to be a calcium channel subunit. TRPC2 is a subunit of a sperm calcium channel that links ZP3 stimulation to sustained intracellular calcium responses that occur during the early stages of fertilization in many animal species. TRPC2-S is a candidate enkurin receptor. The invention includes methods of identifying compds. that affect enkurin expression or activity, and are useful, e.g., for contraception and treatment of infertility.

L9 ANSWER 19 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:687499 CAPLUS
TI Effects of Base Modifications on ***Antisense*** Properties of 2'-O-Methoxyethyl and ***PNA*** Oligonucleotides
AU Sazani, Peter; Astriab-Fischer, Anna; Kole, Ryszard
CS Lineberger Comprehensive Cancer Center & Department of Pharmacology, University of North Carolina, Chapel Hill, NC, 27599, USA
SO Antisense & Nucleic Acid Drug Development (2003), 13(3), 119-128 CODEN: ANADF5; ISSN: 1087-2906
PB Mary Ann Liebert, Inc.
DT Journal
LA English
AB A recently developed ***antisense*** splicing assay was used to det. the relative activities of 2'-O-methoxyethoxy (2'-MOE) phosphorothioate oligonucleotides contg. base modifications. In the assay, RNase H-inactive oligonucleotides are used to block aberrant splicing and restore correct splicing of an Enhanced Green Fluorescence Protein (EGFP) reporter pre-mRNA stably expressed in HeLa cells. Thus, the extent of EGFP upregulation is proportional to the ***antisense*** activity of the tested mol. The base modifications included C-5 propynyl analogs of uridine and cytidine and phenoxazine and G-clamp analogs of cytosine. Base-modified 2'-MOE oligonucleotides were delivered to the HeLa EGFP-654 test cells by cationic lipid transfection or scrape-loading or without any delivery method (free uptake). When delivered with a cationic lipid, the G-clamp and phenoxazine oligomers showed increases in activity over the unmodified 2'-MOE parent compd. However, when delivered by scrape-loading or without a delivery method, the unmodified oligomer performed best. The results suggest that base modifications do not enhance the free uptake activity of RNase H inactive 2'-MOE oligomers.
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 20 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:678975 CAPLUS
DN 139:208746
TI Single-stranded RNA sequence for RNA interference of target genes
IN Suzuki, Mikio; Momota, Hiroshi; Watanabe, Takeshi
PA Otsuka Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 71 pp. CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- -------------- --------
PI WO 2003070932 A1 20030828 WO 2003-JP1913 20030221 W: AU, CA, CN, JP, US RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR
PRAI JP 2002-46889 A 20020222
AB This invention provides a single-stranded polynucleotide sequence which comprises a nucleic acid sequence complementary to the target gene sequence, having RNA interference effect. The sequence comprises consecutive components (I, II, III), having RNA interference effect against the sequence complementary to the components (I) and (III). Component (III) is a sequence complementary to the target gene sequence and (I) is complementary to (III). Component (II) is a nucleotide or non-nucleotide sequence such as ***PNA*** , cytosol localization sequence, sequence with decoy activity, interferon induction suppression sequence, RNase inhibition sequence, sequence with ***antisense*** activity, ribozyme activity, or tRNA. Use of the sequence for gene silencing, drug screening, and as gene therapy agent, is claimed. Knockdown cells, tissues, animals, and plants are claimed. Single-stranded RNA for RNA interference targeting firefly luciferase gene, and lamin A/C gene, were constructed. RNA interference was demonstrated in HeLa cells transfected with those constructs. Amyloid precursor (APP).
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 21 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:678488 CAPLUS
DN 139:214718
TI Chiral peptide nucleic acids with a N-aminoethyl-D-proline backbone
IN Lowe, Gordon
PA UK
SO U.S. Pat. Appl. Publ., 14 pp. CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- -------------- --------
PI US 2003162699 A1 20030828 US 2001-22585 20011030
PRAI US 2001-22585 20011030
OS MARPAT 139:214718
AB Chiral peptide nucleic acids are provided which hybridize strongly with complementary nucleic acids and have potential as antigene and ***antisense*** agents and as tools in mol. biol. The compds. have formula I [n is 1-200; B is an (un)protected base; X is OH or OR2, where R2 is a protecting, activating, or lipophilic group, an amino acid, amino amide, or nucleoside; Y is H or a protecting, lipophilic, or aminoacyl group or a nucleoside; R, R1 are H, alkyl, aryl, or aralkyl or may form a cycloalkyl ring]. Thus, H-[(.PSI.-CH2)Gly-D-Pro(T)]10-Lys-NH2 was prepd. and complexed with oligonucleotides [Tm = 53.degree. for complex with poly(rA)].

L9 ANSWER 22 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:651965 CAPLUS
TI Sensitization and apoptosis augmentation of K562/ ADM cells by anti-multidrug resistance gene ***peptide*** ***nucleic*** ***acid*** and ***antisense*** oligodeoxyribonucleotide
AU Wei, Hu-Lai; Wu, Yong-Jie; Jing, Tao; Bai, De-Cheng; Ma, Lan-Fang
CS Key Laboratory of Preclinical Study for New Chinese Traditional Drugs of Gansu Province, Lanzhou Medical College, Lanzhou, 730000, Peop. Rep. China

SO Acta Pharmacologica Sinica (2003), 24(8), 805-811 CODEN: APSCG5; ISSN: 1671-4083
PB Science Press
DT Journal
LA English
AB Aim: To investigate the reversal effect and apoptosis enhancement of ***peptide*** ***nucleic*** ***acid*** (***PNA***) and ***antisense*** oligodeoxyribonucleotide (ASODN) targeted to multidrug resistance gene (mdr1) on human multidrug resistant leukemia K562/ADM cells. Methods: A 15-mer ***PNA*** and the same sequence of ASODN, complementary to the 5' end of the AUG initiator codon-contg. region of mdr1 mRNA (MDR1- ***PNA*** , MDR1-ASODN), were designed and synthesized. Proliferation and sensitivity to adriamycin of K562/ADM cells treated with MDR1- ***PNA*** -and MDR1-ASODN were analyzed with a MTT colorimetric assay. Apoptotic morphologies, P-glycoprotein (P-gp) expression, intracellular adriamycin accumulation, and cell cycle were measured. Results: MDR1- ***PNA*** 1 to 10 .mu.mol/L and MDR1-ASODN 2 to 20 .mu.mol/L alone had no inhibitory effects on the proliferation of K562/ADM cells, but significantly inhibited the growth of K562/ADM cells cultured in adriamycin-contg. medium. After treatment with MDR1- ***PNA*** and MDR1-ASODN, intracellular adriamycin accumulation in K562/ADM cells increased greatly and P-gp synthesis was strikingly reduced. The resistance to adriamycin of the drug-resistant cells was partly reversed and the cells were induced to apoptosis by adriamycin. The reversal efficacy of MDR1- ***PNA*** was 3.1-fold higher than that of the same sequence of MDR-ASODN, but neither MDR1- ***PNA*** nor MDR1-ASODN could completely block the mdr1/P-gp expression. Conclusion: Sequence-special ***PNA*** targeted to mdr1 gene more effectively than the same sequence of MDR1-ASODN inhibited the expression of P-glycoprotein to overcome the drug-resistance.
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 23 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:631234 CAPLUS
TI Hybridization of complementary and homologous ***peptide*** ***nucleic*** ***acid*** probes to folded DNA targets
AU Armitage, Bruce A.; Kushon, Stuart A.; Datta, Bhaskar; Schmitt, Christoph; Jordan, Jason P.
CS Department of Chemistry, Carnegie Mellon University, Pittsburgh, PA, 15213-3890, USA
SO Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003 (2003), COMP-074 Publisher: American Chemical Society, Washington, D. C. CODEN: 69EKY9
DT Conference; Meeting Abstract
LA English
AB Folding of natural DNA and RNA sequences imposes thermodn. barriers to hybridization by ***antisense*** agents. This lecture will focus on the thermodn. of hybridization in two model folded structures: a DNA hairpin and a DNA quadruplex. The hairpin forms when two complementary sequences are sepd. by a short noncomplementary region. DNA quadruplexes can arise from folding of guanine-rich sequences. The basic unit of the quadruplex is a guanine tetrad, in which four guanines are simultaneously hydrogen bonded into a square array. Stacking of G-tetrads is facilitated by cation binding. Complementary ***peptide*** ***nucleic*** ***acid*** (***PNA***) probes were synthesized to target these structures and the thermodn. of hybridization were measured using temp.-dependent UV absorbance expts. In addn., a quadruplex-forming DNA was targeted using a homologous, rather than complementary, ***PNA*** probe. The ***PNA*** successfully recognized the G-rich DNA and formed a hybrid PNA2-DNA2 quadruplex, representing the first demonstration of homologous hybridization.

L9 ANSWER 24 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:614894 CAPLUS
TI Synthesis of the ***peptide*** ***nucleic*** ***acid*** analogues by the multi- component condensation reaction I. ***PNA*** monomers synthesis
AU Zhang, Ting; Xu, Ping
CS Department of Medicinal Chemistry, School of Pharmaceutical Sciences, Peking University, Beijing, 100083, Peop. Rep. China
SO Zhongguo Yaowu Huaxue Zazhi (2002), 12(6), 325-328 CODEN: ZYHZEF; ISSN: 1005-0108
PB Zhongguo Yaowu Huaxue Zazhi Bianjibu
DT Journal
LA Chinese
AB The Ugi-4CC reaction for synthesizing the ***PNA*** (***peptide*** ***nucleic*** ***acid*** , a new type of the ***antisense*** compd. family as biol. probe for diagnosis and treatment of diseases) analog monomer was presented. N-(2-tert-butoxycarbonylethyl)-2-[N'-(3- methylbutyl)-2-(1-thyminyl)acetamido]acetamide was synthesized from thymin-1-ylacetic acid, formaldehyde, 3-methylbutanamine, and 2-tert-butoxycarbonylaminoethyl isocyanide. The structures were confirmed by MS, IR, 1H-NMR spectra, and elemental anal.

L9 ANSWER 25 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:599815 CAPLUS
TI 99mTc-peptide- ***peptide*** ***nucleic*** ***acid*** probes for imaging oncogene mRNAs in tumours
AU Rao, P. S.; Tian, X.; Qin, W.; Aruva, M. R.; Sauter, E. R.; Thakur, M. L.; Wickstrom, E.
CS Department of Radiology, Thomas Jefferson University, Philadelphia, PA, 19107, USA
SO Nuclear Medicine Communications (2003), 24(8), 857-863 CODEN: NMCODC; ISSN: 0143-3636
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB SUMMARY: Imaging oncogene mRNA in tumors would provide a powerful tool for the early detection of occult malignant lesions. The goal was to prep. a chimera consisting of a dodecamer ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***) specific for c-MYC oncogene overexpressed in human breast cancer cells and a chelating moiety that facilitates quant. radiolabelling with 99mTc and evaluate it for hybridization and tissue distribution in lab. animals. The pentapeptide chelator-***PNA*** dodecamer specific for c-MYC mRNA was extended from a solid support by 9-fluorenylmethyloxycarbonyl (Fmoc) coupling. Similarly, a chelator- ***PNA*** chimera with four central mismatches was also prepd. which served as a control. The chimeras were purified, characterized and evaluated for hybridization to c-MYC mRNA by fluorescent, real-time polymerase chain reaction (RT-PCR). The chimeras were labeled with 99mTc and their tissue distribution was examd. in athymic nude mice bearing exptl. human breast tumors. 99mTc radiolabelling was quant. and presented a single peak in reversed phase liq. chromatog. Fluorescent real-time polymerase chain reactions using primer and fluorescent probe sets previously calcd. for c-MYC mRNA demonstrated inhibition of reverse transcription by the c-MYC specific chimera as compared to that of the control. Tissue distribution studies of ***antisense*** and mismatch chimeras at 4 h and 24 h after administration displayed modest accumulation in the liver, and appreciable levels in tumors. These observations suggest that 99mTc-peptide-

PNA probes might be useful for imaging gene expression in tumors, and the approach is worthy of further investigation.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 26 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:596290 CAPLUS
DN 139:161307
TI Preparation of ***antisense*** ***peptide*** ***nucleic*** ***acid*** exhibiting high affinity to RNA and the use of the ***PNA*** in gene therapy
IN Mohammed, Abdul-Aziz Ozman; Yamazaki, Tetsuro; Otsuka, Masaki
PA Mitsubishi Rayon Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 18 pp. CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI JP 2003219874 A2 20030805 JP 2002-20646 20020129
PRAI JP 2002-20646 20020129
OS MARPAT 139:161307
AB This invention provides a process of prepn. of ***antisense*** ***peptide*** ***nucleic*** ***acid*** (I, R1 = H, protecting group of amino group; R2 = protecting group of hydroxyl group, protecting group of carboxyl group; R3 = direct coupling, Me group, ethylene group; B = base and m = 1-60) exhibiting high affinity to RNA. The monomer ***PNA*** (III, IV, R1 = H, protecting group of amino group; R2 = protecting group of hydroxyl group, protecting group of carboxyl group and B = base) were prepd. from (II, R1 = H, protecting group of amino group). The ***antisense*** ***PNA*** provided in this invention can be used in gene therapy.

L9 ANSWER 27 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:577245 CAPLUS
TI Selective inhibition of inducible cyclo-oxygenase-2 expression by ***antisense*** peptide nucleic acids in intact murine macrophages
AU Scarfi, Sonia; Giovine, Marco; Pintus, Raffaela; Millo, Enrico; Clavarino, Emanuela; Pozzolini, Marina; Sturla, Laura; Stock, Roberto Pablo; Benatti, Umberto; Damonte, Gianluca
CS Biochemistry Section, Department of Experimental Medicine, University of Genoa, Genoa, 16132, Italy
SO Biotechnology and Applied Biochemistry (2003), 38(1), 61-69 CODEN: BABIEC; ISSN: 0885-4513
PB Portland Press Ltd.
DT Journal
LA English
AB Prostaglandins are important mols. involved in inflammation and immunomodulation. The rate-limiting step in the synthesis of these potent mediators is the expression of the enzyme cyclo-oxygenase (COX). The isoform responsible, COX-2, is encoded by an immediate-early gene induced by various pro-inflammatory agents in macrophages. Selective blockade of COX-2 by the use of an ***antisense*** strategy would overcome the undesirable side effects of conventional inhibitors. Here we describe cellular internalization and activity of a novel class of oligonucleotide analogs named peptide nucleic acids (PNAs) as inhibitors of COX-2 translation. In particular, we designed two ***antisense*** murine COX-2 ***PNA*** mols., directed against a mRNA region spanning the AUG translation-initiation codon and a homopurinic sequence inside the COX-2 mRNA reading frame. These two ***PNA*** sequences, used sep. or mixed together, demonstrated the capacity to inhibit the translation of murine COX-2 enzyme in a cell-free translation model using a rabbit retculocyte lysate model. Since PNAs display very low natural permeability across lipids bilayers, the two mols. were also re-synthesized, modified to be used in intact cells by means of linkage to a hydrophobic peptide to obtain membrane-diffusable ***PNA*** chimaerae. Finally, stimulated macrophages were found to be affected strongly by these two compds., used sep. or together, monitoring inhibition of COX-2 synthesis by Western blot anal. of total lysates and enzymic activity via radioactive assay on the microsomal fractions.
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 28 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:570852 CAPLUS
DN 139:111619
TI Conjugates of membrane-penetrating peptides and therapeutic compounds for treatment of infection by antibiotic-resistant prokaryotes
IN Braun, Klaus; Braun, Isabell; Debus, Juergen; Pipkorn, Ruediger; Waldeck, Waldemar
PA Deutsches Krebsforschungszentrum Stiftung des Oeffentlichen Rechts, Germany
SO PCT Int. Appl., 34 pp. CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2003059392 A2 20030724 WO 2003-DE124 20030117 WO 2003059392 A3 20031023 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG DE 10201862 A1 20030807 DE 2002-10201862 20020118
PRAI DE 2002-10201862 A 20020118
AB The invention relates to a conjugate for delivery of a therapeutic agent into a prokaryotic cell for the treatment of prokaryotic infections. The conjugate is of a peptide that can penetrate a prokaryotic cell membrane, such as a defensin, and a therapeutic moiety. The therapeutic moiety is preferably a ***peptide*** ***nucleic*** ***acid*** (***PNA***), which is directed against a gene of the prokaryote that imparts a resistance to antibiotics. Disulfide-bridged conjugates of defensin, a peptide linker, and a ***PNA*** directed against a kanamycin resistance gene were synthesized. Kanamycin-resistant Escherichia coli treated with the conjugated became kanamycin sensitive. The conjugate was not toxic to HeLa cells.

L9 ANSWER 29 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:570238 CAPLUS
DN 139:317964
TI Effects of ***antisense*** ***peptide*** ***nucleic*** ***acid*** to platelet-derived growth factor A-chain on growth of vascular smooth muscle cells
AU Fukuda, Noboru; Furuya, Rie; Kishioka, Hirobumi; Suzuki, Ryo; Matsuda, Hiroyuki; Tahira, Yoshiko; Takagi, Hiroto; Ikeda, Yukihiro; Saito, Satoshi; Matsumoto, Koichi; Kanmatsuse, Katsuo
CS Second Dep. Internal Medicine, Nihon Univ. Sch. Medicine, Tokyo, Japan
SO Journal of Cardiovascular Pharmacology (2003), 42(2), 224-231 CODEN: JCPCDT; ISSN: 0160-2446
PB Lippincott Williams & Wilkins

DT Journal
LA English
AB To investigate ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***) as a gene therapy for the arterial proliferative diseases, the authors designed and examd. the effects of an ***antisense*** ***PNA*** targeting platelet-derived growth factor (PDGF) A-chain on expression of PDGF A-chain and growth of vascular smooth muscle cells (VSMCs) from spontaneously hypertensive rats. A 15-mer ***antisense*** ***PNA*** complementary to the initiation codon of rat and human PDGF A-chain mRNA was synthesized and purified by HPLC. Gel-shift assay and biomol. interaction anal. (BIAcore) revealed that the ***antisense*** ***PNA*** bound weakly to the target RNA, whereas it bound strongly to the target DNA. Fluorescein-isothiocyanate-labeled ***antisense*** ***PNA*** to PDGF A-chain was taken up slowly and maintained in VSMCs for a prolonged period of time. ***Antisense*** ***PNA*** inhibited expression of PDGF A-chain mRNA and protein as well as DNA synthesis in VSMCs in a dose-independent manner. Inhibition of DNA synthesis by the ***antisense*** ***PNA*** was greater than that by the ***antisense*** DNA at a low concn. (5 .mu.M). These results suggest that ***antisense*** ***PNA*** to PDGF A-chain will be used as a gene therapy for vascular proliferative diseases such as hypertensive vascular diseases, restenosis of coronary arteries after angioplasty, and atherosclerosis.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 30 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:568595 CAPLUS
DN 139:130426
TI Diagnostic conjugate consisting of a transmembrane transport module, ***antisense*** ***PNA*** , and signaling module for intercellular expression profile imaging of genes in tumor cells
IN Braun, Klaus; Debus, Juergen; Jenne, Juergen; Heckl, Stefan; Pipkorn, Ruediger; Rastert, Ralf; Waldeck, Waldemar; Braun, Isabell
PA Deutsches Krebsforschungszentrum Stiftung Des Oeffentlichen Rechts, Germany
SO Eur. Pat. Appl., 16 pp. CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- -------------- --------
PI EP 1329227 A1 20030723 EP 2002-1506 20020122 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR WO 2003061712 A1 20030731 WO 2003-EP609 20030122 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI EP 2002-1506 A 20020122
AB The present invention provides a diagnostic conjugate comprising (a) a transmembrane module (TPU), (b) an addressing module (AS), preferably an ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***), and (c) a signaling module (SM) allowing to det., e.g. by MRI, the expression profile of genes of interest, e.g. genes the expression of which differs between tumor cells and non tumor cells. In the expts. leading to the present invention, the intracellular uptake of the commonly used interstitial contrast agent gadolinium was improved by building an ***Antisense*** -Conjugated-Gadolinium-Transporter (ACGT) consisting of a transmembrane transport module (TPU), an address module (c-myc mRNA directed ***antisense*** -sequence) and the Gd3+ complex module. The so-called ***antisense*** -principle was used to realize a differentiation between tumor and non-tumor cells in MRI. Based on the differing gene expression patterns seen in tumor cells as compared to normal cells, the target-specific ***Antisense*** -Conjugated- Gadolinium-Transporter (ACGT) contg. an ***antisense*** -sequence (***Antisense*** = AS; Table 1) which is covalently bound to a transport-peptide (TPU) of human origin, and thus does not have any effect on transactivating properties was highly useful. The virtually peptidase- and nuclease resistant modified oligonucleotides (PNAs) are complementary sequences which are bound to the Gd-transporter-complex targeted at c-myc mRNA. Upon contact of the ***antisense*** -conjugated-gadolinium- transporter (ACGT) contg. c-myc-targeted peptide nucleic acids (PNAs) with c-myc mRNA in the cytoplasm, a hybrid is formed composed of ***PNA*** and RNA. This hybrid begins to be slowly enzymically cleaved after 24 h and the ACGT then starts to leave the cell, effectively causing a delayed efflux. In cells in which c-myc mRNA is hardly present (lymphocytes and other normal cells) there is no detectable hybridization, the efflux process is immediately initiated and causes a more rapid redn. in intracellular Gd-complex concn. Using Magnetic Resonance Imaging (MRI), Gadolinium was detected within HeLa cervix-carcinoma cells as well as non-tumor cells (lymphocytes) already after 10 min. The ACG-transporter was rapidly released from non-tumor cells, whereas, in HeLa cells, only a minimal efflux was obsd. This suffices for a clear differentiation between tumor and nontumor cells.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 31 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:566285 CAPLUS
TI ***Peptide*** ***nucleic*** ***acid*** (***PNA***): A DNA mimic with a pseudopeptide backbone
AU Beck, Frederik; Nielsen, Peter E.
CS Pantheco A/S, Copenhagen, Den.
SO Artificial DNA (2003), 91-114. Editor(s): Khudyakov, Yuri E.; Fields, Howard A. Publisher: CRC Press LLC, Boca Raton, Fla. CODEN: 69EGFC; ISBN: 0-8493-1426-7
DT Conference; General Review
LA English
AB A review discusses the introduction of ***peptide*** ***nucleic*** ***acid*** , a DNA mimic with a pseudopeptide backbone, for the development of gene therapeutic ***antisense*** and antigene drugs, genetic diagnostics, and mol. tools as well as in bioorg. chem. for studying biomol. recognition and DNA structure and function. ***PNA*** is truly an artificial DNA in terms of structure but not in terms of biol. function.
RE.CNT 127 THERE ARE 127 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 32 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:565641 CAPLUS
DN 139:112706
TI ***Antisense*** oligodeoxynucleotide against the pituitary tumor transforming gene (PTTG) for inhibition of translation in human cells
IN Roller, Marc

PA Germany
SO Ger. Offen., 6 pp. CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI DE 10200410 A1 20030724 DE 2002-10200410 20020108
PRAI DE 2002-10200410 20020108
AB The invention relays to the inhibition of pituitary tumor transforming gene (PTTG) mRNA translation by means of ***antisense*** oligodeoxynucleotides. The invention concerns the use of oligodeoxynucleotides for inhibition of PTTG transcription, which effectively can inhibit the growth of PTTG overexpressed tumor cells. PTTG-1 overexpression is described for a set of tumors and tumor cell lines. PTTG was described as overexpressed for the first time in rat pituitary gland tumors. An overexpression by means of stable transfection in NIH-3T3 mouse fibroblasts leads to cell transformation in vitro and to the formation of solid tumors in vivo. The inhibition of PTTG-1 by means of ***antisense*** ODNs leads extensive proliferation inhibition in human HeLa-S3 tumor cells.
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 33 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:538713 CAPLUS
TI ***Peptide*** ***nucleic*** ***acid*** and gene therapy
AU Zhou, Yanling; Qin, Huaming; Xie, Zhenwen
CS Department of Agronomy, Zhongkai Agricultural Technology College, Canton, 510225, Peop. Rep. China
SO Guangdong Yaoxueyuan Xuebao (2003), 19(1), 64-66 CODEN: GYXUF8
PB Guangdong Yaoxueyuan
DT Journal; General Review
LA Chinese
AB A review with 17 refs. on ***peptide*** ***nucleic*** ***acid*** (***PNA***) and gene therapy with emphasis on the structure and binding characteristics of ***PNA*** and application of ***PNA*** as genetically therapeutic agent (such as ***antisense*** drug, gene transfer carrier, and inducer for endogenous gene expression).

L9 ANSWER 34 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:522157 CAPLUS
TI Peptide-mediated cellular delivery of ***antisense*** oligonucleotides and their analogues
AU Gait, Michael J.
CS Laboratory of Molecular Biology, Medical Research Council, Cambridge, CB2 2QH, UK
SO Cellular and Molecular Life Sciences (2003), 60(5), 844-853 CODEN: CMLSFI; ISSN: 1420-682X
PB Birkhaeuser Verlag
DT Journal
LA English
AB Improving the delivery of synthetic oligonucleotides and their analogs into cells is an important goal in the full development of ***antisense*** technol. for control of gene expression in cell culture and in vivo. This review describes the harnessing of certain peptides, either as noncovalent complexes or as covalent conjugates, to enhance the delivery of ***antisense*** oligonucleotides into cells and/or to affect their cell localization. Phosphodiester and phosphorothioate oligonucleotides are included as well as peptide nucleic acids (PNAs), analogs of oligonucleotides where the neg. charged phosphate backbone is replaced by a neutral amide linkage. This review contains a crit. evaluation of claims for certain peptide-oligonucleotide conjugates to translocate into cultured cells by a non-energy-dependent nonendosomal route. In addn., the available evidence for the utility of stable vs. nonstable linkages between peptide and oligonucleotide or ***PNA*** is discussed.
RE.CNT 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 35 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:505868 CAPLUS
TI Photochemical Internalization of a ***Peptide*** ***Nucleic*** ***Acid*** Targeting the Catalytic Subunit of Human Telomerase
AU Folini, Marco; Berg, Kristian; Millo, Enrico; Villa, Raffaella; Prasmickaite, Lina; Daidone, Maria Grazia; Benatti, Umberto; Zaffaroni, Nadia
CS Department of Experimental Oncology, Istituto Nazionale per lo Studio e la Cura dei Tumori di Milano, Milan, 20133, Italy
SO Cancer Research (2003), 63(13), 3490-3494 CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Because peptide nucleic acids (PNAs) are poorly taken up by mammalian cells, strategies need to be developed for their intracellular delivery. In the present study, we demonstrated the possibility to efficiently release a naked ***PNA*** targeting the catalytic component of human telomerase reverse transcriptase (hTERT- ***PNA***) into the cytoplasm of DU145 prostate cancer cells through the photochem. internalization approach. After light exposure, cells treated with the hTERT- ***PNA*** and photosensitizer TPPS2a showed a marked inhibition of telomerase activity and a reduced cell survival, which was not obsd. after treatment with hTERT- ***PNA*** alone. Moreover, in a direct comparison, photochem. internalization technol. proved to be more efficient to internalize the hTERT- ***PNA*** than an HIV-Tat protein-based approach.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 36 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:485894 CAPLUS
DN 139:240202
TI Design and application of a ***peptide*** ***nucleic*** ***acid*** sequence targeting the p75 neurotrophin receptor
AU Cheah, Irwin K.; Cheema, Surindar S.; Langford, Steven J.; Lopes, Elizabeth C.; MacFarlane, Katherine J.; Petratos, Steven; Turner, Bradley J.
CS School of Chemistry, Monash University, Victoria, 3800, Australia
SO Bioorganic & Medicinal Chemistry Letters (2003), 13(14), 2377-2380 CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science B.V.
DT Journal
LA English
AB Novel ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***) constructs targeting p75NTR as a potential therapeutic strategy for amyotrophic lateral sclerosis (ALS) were designed, synthesized and evaluated against phosphorothioate oligonucleotide sequences (PS-ODN). An 11-mer ***antisense*** ***PNA*** directed at the initiation codon dose-dependently inhibited p75NTR expression and death signaling by nerve growth factor in Schwann cell cultures. Inhibition of p75NTR prodn. was not detected in cultures treated with the nonsense ***PNA*** or ***antisense*** ***PNA*** directed at the 3'-terminus sequence. The 19-mer PS-ODN sequences also failed to confer any activity against p75NTR but, unlike the ***PNA*** sequences, were toxic in vitro at comparable doses.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 37 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:458305 CAPLUS
TI A rapid coupling protocol for the synthesis of peptide nucleic acids
AU Vearing, Christopher J.; Fecondo, John V.
CS School of Engineering and Science, Swinburne University of Technology, Hawthorn, Victoria, Australia
SO Letters in Peptide Science (2003), Volume Date 2002, 9(4-5), 211-219 CODEN: LPSCEM; ISSN: 0929-5666
PB Kluwer Academic Publishers
DT Journal
LA English
AB With the current interest in ***anti*** - ***sense*** and anti-gene technologies, an efficient, fast and less toxic synthesis protocol would be advantageous for the oligomerisation of Peptide Nucleic Acids (***PNA***). Most of the methods currently in use for the t-Boc synthesis of ***PNA*** 's use TFA/m-cresol, pyridine, piperidine and capping reagents. In this work, a rapid synthesis protocol has been adapted from an earlier published peptide synthesis method allowing a redn. in cycle time from around 30 min down to 16 min. By utilizing quant. deprotection with 100% TFA, a coupling time of 10 min and a four-fold excess of monomer, this synthesis protocol has been used to synthesize a no. of ***PNA*** 's incorporating all four nucleotides of varying sequence, up to 17 residues in length.

L9 ANSWER 38 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:454163 CAPLUS
DN 139:30785
TI Thermally activated conjugates of clasp peptide nucleic acids with transport proteins for therapeutic control of gene expression
IN Braun, Klaus; Braun, Isabell; Corban-Wilhelm, Heike; Debus, Juergen; Jenne, Juergen; Rastert, Ralf; Pipkorn, Ruediger; Simiantonakis, Ioannis; Waldeck, Waldemar
PA Deutsches Krebsforschungszentrum Stiftung Des Oeffentlichen Rechts, Germany
SO PCT Int. Appl., 27 pp. CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2003047631 A2 20030612 WO 2002-DE4356 20021127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG DE 10158331 A1 20030612 DE 2001-10158331 20011128
PRAI DE 2001-10158331 A 20011128
AB The invention concerns conjugates of peptide-nucleic acids for inhibition of gene expression in the treatment of disease. The peptide nucleic acids are conjugated with a moiety that will stimulate cell uptake, such as a penetratin, another that targets the conjugate to the tumor cell, and a nuclear localization signal. The ***peptide*** ***nucleic*** ***acid*** is in an inactive clasp configuration, such as a triple helix, that denatures at an elevated temp., e.g. during a fever or by therapeutic hyperthermia, to denature a complex that may release an RNA or an ***antisense*** sequence. The peptide components may be connected by peptide bonds or disulfide bridges. Thermal regulation of expression of a gene for green fluorescent protein in animal cell culture is demonstrated. The clasp had a denaturation temp. of 44.degree. and a sharp induction of fluorescence could be seen when transformed cells were cultured at temps. >43.degree..

L9 ANSWER 39 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:432117 CAPLUS
TI Targeting of folded nucleic acids with complementary and homologous ***PNA*** hybridization probes
AU Armitage, Bruce A.
CS Department of Chemistry, Mellon College of Science, Carnegie Mellon University, Pittsburgh, PA, USA
SO Abstracts, 31st Northeast Regional Meeting of the American Chemical Society, Saratoga Springs, NY, United States, June 15-18 (2003), 45 Publisher: American Chemical Society, Washington, D. C. CODEN: 69EBFV
DT Conference; Meeting Abstract
LA English
AB The ***antisense*** strategy for regulating gene expression is well established in the lab. and one ***antisense*** drug has reached the clinic. This approach involves hybridization between the ***antisense*** agent and its complementary sequence within the target RNA. A potential complication in this approach is restricted access of the ***antisense*** agent to its target sequence due to folding of the RNA. Aside from the kinetic implications of RNA folding on hybridization, thermodn. penalties will be incurred due to the energetic cost of unfolding the RNA in order to access the target sequence. This lecture will focus on the thermodn. of hybridization in two model folded structures: a DNA hairpin and a DNA quadruplex. The hairpin forms when two complementary sequences are sepd. by a short noncomplementary region. DNA quadruplexes can arise from folding of guanine-rich sequences. The basic unit of the quadruplex is a guanine tetrad, in which four guanines are simultaneously hydrogen bonded into a square array. Stacking of G-tetrads is facilitated by cation binding. Complementary ***peptide*** ***nucleic*** ***acid*** (***PNA***) probes were synthesized to target these structures and the thermodn. of hybridization were measured using temp.-dependent UV absorbance expts. In addn., a quadruplex-forming DNA was targeted using a homologous, rather than complementary, ***PNA*** probe. The ***PNA*** successfully recognized the G-rich DNA and formed a hybrid PNA2-DNA2 quadruplex, representing the first demonstration of homologous hybridization.

L9 ANSWER 40 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:395330 CAPLUS
DN 139:130034
TI Peptide- ***PNA*** conjugates: targeted transport of ***antisense*** therapeutics into tumors
AU Mier, Walter; Eritja, Ramon; Mohammed, Ashour; Haberkorn, Uwe; Eisenhut, Michael
CS Univ. Heidelberg Radiologische Klinik, Abteilung Nuklearmedizin Im Neuenheimer Feld 400, Heidelberg, 69120, Germany
SO Angewandte Chemie, International Edition (2003), 42(17), 1968-1971 CODEN: ACIEF5; ISSN: 1433-7851
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
AB The success of using gene therapy to treat cancer patients depends on the development of a new vector system that enables transport of high mol. wt. substances such as oligonucleotides. Since it has not been possible to selectively transport ***antisense*** oligonucleotides into tumor cells, the

question arose whether it would be possible to use somatostatin-receptors (SSTR)-affine peptides as carriers for oligonucleotides. Using metabolically stable peptide nucleic acids (PNAs), the convergence of ***PNA*** and peptide synthesis was found to enable the stepwise synthesis of ***PNA*** -peptide conjugates on the same polymeric support. Either 9-fluorenylmethoxycarbonyl (Fmoc) or tert-butyloxycarbonylchem. are suitable for the synthesis of ***PNA*** oligomers. However, due to side reactions during deprotection of the Fmoc protecting group, the purity of the products produced by Boc chem. is higher. The ***PNA*** oligomers can be synthesized by using Boc chem. in good yields, consequently this method is also suitable for the synthesis of ***PNA*** -peptide conjugates. During chain elongation in peptide and ***PNA*** synthesis, aggregation of the growing oligomer chain can be caused by either intra- or intermol. interactions. This may lead to a collapse of the solid support and thus to low coupling efficiencies. The physicochem. properties of the ***PNA*** -peptide conjugate are different to those of the Tyr3-octreotide. These properties influence factors like the interaction with serum proteins and result in different organ uptake, in particular in the kidney, the liver, and the lung. The modification of the ***PNA*** with the peptide part led to an about tenfold increase in tumor uptake. RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 41 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:282303 CAPLUS
DN 138:316490
TI Nucleic acid molecules, polypeptides and uses therefor, including diagnosis and treatment of Alzheimer's disease in human
IN Durham, L. Kathryn; Friedman, David L.; Herath, Herath Mudiyanselage Athula Chandrasiri; Kimmel, Lida H.; Parekh, Rajesh Bhikhu; Potter, David M.; Rohlff, Christian; Silber, B. Michael; Snyder, Peter Jeffrey; Soares, Holly Daria; Stiger, Thomas R.; Sunderland, P. Trey; Townsend, Robert Reid; White, W. Frost; Williams, Stephen A.
PA Pfizer Products Inc., USA; Oxford Glycosciences (Uk) Ltd.
SO PCT Int. Appl., 179 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2003028543 A2 20030410 WO 2002-US31642 20021003
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG JP 2003284574 A2 20031007 JP 2002-291568 20021003
PRAI US 2001-326708P P 20011003
AB The present invention provides methods and compns. for screening, diagnosis and prognosis of Alzheimer's disease, for monitoring the effectiveness of Alzheimer's disease treatment, and for drug development. The invention relates to the identification of protein and protein isoforms that are assocd. with predisposition to Alzheimer's Disease and its onset and development, and of genes and nucleic acid mols., encoding the same, and to their use for e.g., clin. screening, diagnosis, treatment, as well as for drug screening and drug development. Alzheimer's Disease-Assocd. features (AFs), detectable by two-dimensional electrophoresis of cerebrospinal fluid, serum or plasma are described. The invention further provides Alzheimer's Disease-Assocd. Protein Isoforms (APIs) detectable in cerebrospinal fluid, serum or plasma, prepns. comprising isolated APIs antibodies immunospecific for APIs, pharmaceutical compns., diagnostic and therapeutic methods, and kits comprising or based on the same.

L9 ANSWER 42 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:276220 CAPLUS
TI ***PNA*** and oligonucleotide inhibitors of human telomerase
AU Gavory, Gerald; Balasubramanian, Shankar
CS Department of Chemistry, University of Cambridge, Cambridge, UK
SO Molecular Biology Intelligence Unit (2002), 22(Telomerases, Telomeres and Cancer), 100-113 CODEN: MBIUF8; ISSN: 1431-0414
PB Landes Bioscience
DT Journal; General Review
LA English
AB A review describes the ***antisense*** inhibition of human telomerase using oligonucleotide analogs. The ***antisense*** approach is the inactivation of gene expression at the transcriptional lelvel typically using a short oligonucleotide or mimic to target a complementary sequence of the corresponding mRNA. The most potent oligonucleotide analog include phosphorothioate DNA, 2'-O-alkyl RNA and peptide nucleic acids (***PNA***). ***PNA*** oligomers bind complementary sequence with high affinity relative to analogous DNA or RNA. ***PNA*** /RNA hybrids also exhibit higher thermal stability compared to the corresponding DNA/DNA or DNA/RNA duplex. RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 43 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:274524 CAPLUS
DN 138:287961
TI Development of ***antisense*** .alpha.-helical peptide nucleic acids
AU Huang, Yumei
CS Case Western Reserve Univ., Cleveland, OH, USA
SO (2002) 278 pp. Avail.: UMI, Order No. DA3058345 From: Diss. Abstr. Int., B 2003, 63(7), 3299
DT Dissertation
LA English
AB Unavailable

L9 ANSWER 44 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:126806 CAPLUS
DN 139:254676
TI Direct ***peptide*** ***nucleic*** ***acid*** uptake in human dendritic cells
AU Li, S.; Feng, G.; Li, Y.; Bu, H.; Lu, Y.; Yang, Y.
CS West China Hospital, Lab of Transplant Engineering and Immunology, Sichuan University, Sichuan, Peop. Rep. China
SO Transplantation Proceedings (2003), 35(1), 550-552 CODEN: TRPPA8; ISSN: 0041-1345
PB Elsevier Science Inc.
DT Journal
LA English
AB Treatment of dendritic cells with ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***) targeting mRNA of costimulatory mols. may enhance tolerogenicity. This report describes uptake and action of ***antisense*** ***PNA*** to CD86 mRNA into dendritic cells.

PNA was found to be internalized by dendritic cells within minutes, specially depressing the expression of its target mRNA.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 45 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:78794 CAPLUS
DN 138:151990
TI ***Peptide*** ***nucleic*** ***acid*** ***antisense*** prolongs skin allograft survival by means of blockade of CXCR3 expression directing T cells into graft
AU Ming, Jiankuo; Wang, Xingbing; Huang, Baojun; Wu, Xiongwin; Li, Zhuoya; Xiong, Ping; Xu, Yong; Liu, Anting; Hu, Chunsong; Gong, Feili; Tan, Jinquan
CS Department of Immunology, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Peop. Rep. China
SO Journal of Immunology (2003), 170(3), 1556-1565 CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB CXCR3, predominantly expressed on memory/activated T cells, is a receptor for both IFN-.gamma.-inducible protein 10/CXC chemokine ligand (CXCL)10 and monokine induced by IFN-.gamma./CXCL9. It was reported that CXC chemokines IFN-.gamma.-inducible protein 10/CXCL10 and monokine induced by IFN-.gamma./CXCL9 play a crit. role in the allograft rejection. The authors report that CXCR3 is a dominant factor directing T cells into mouse skin allograft, and that ***peptide*** ***nucleic*** ***acid*** (***PNA***) CXCR3 ***antisense*** significantly prolongs skin allograft survival by blockade of CXCR3 expression directing T cells into allografts in mice. The authors found that CXCR3 is highly up-regulated in spleen T cells and allografts from BALB/c recipients by day 7 of receiving transplantation, whereas CCR5 expression is moderately increased. The authors designed ***PNA*** CCR5 and ***PNA*** CXCR3 antisenses, and i.v. treated mice that received skin allograft transplantations. The ***PNA*** CXCR3 at a dosage of 10 mg/kg/day significantly prolonged mouse skin allograft survival (17.1 days) compared with physiol. saline treatment (7.5 days), whereas ***PNA*** CCR5 (10 mg/kg/day) marginally prolonged skin allograft survival (10.7 days). The mechanism of prolongation of skin allograft survival is that ***PNA*** CXCR3 directly blocks the CXCR3 expression in T cells, which is responsible for directing T cells into skin allograft to induce acute rejection, without interfering with other functions of the T cells. These results were obtained at mRNA and protein levels by flow cytometry and real-time quant. RT-PCR technique, and confirmed by chemotaxis, Northern and Western blot assays, and histol. evaluation of skin grafts. The present study indicates the therapeutic potential of ***PNA*** CXCR3 to prevent acute transplantation rejection.
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 46 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:66601 CAPLUS
DN 138:297094
TI Correction of disease-associated exon skipping by synthetic exon-specific activators
AU Cartegni, Luca; Krainer, Adrian R.
CS Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 11724, USA
SO Nature Structural Biology (2003), 10(2), 120-125 CODEN: NSBIEW; ISSN: 1072-8368
PB Nature Publishing Group
DT Journal
LA English
AB Differential exon use is a hallmark of alternative splicing, a prevalent mechanism for generating protein isoform diversity. Many disease-assocd. mutations also affect pre-mRNA splicing, usually causing inappropriate exon skipping. SR proteins are essential splicing factors that recognize exonic splicing enhancers and drive exon inclusion. To emulate this function of SR proteins, we designed small chimeric effectors comprising a minimal synthetic RS domain covalently linked to an ***antisense*** moiety that targets an exon by Watson-Crick base pairing. Here we show that such synthetic effectors can mimic the functions of SR proteins and specifically restore wild type splicing when directed to defective BRCA1 or SMN2 pre-mRNA transcripts. This general approach can be used as a tool to investigate splicing mechanisms and modulate alternative splicing of specific genes, and as a therapeutic strategy to correct splicing defects responsible for numerous diseases.
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 47 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:64521 CAPLUS
DN 139:312006
TI Cellular delivery of ***peptide*** ***nucleic*** ***acid*** (***PNA***)
AU Koppelhus, Uffe; Nielsen, Peter E.
CS Department of Medical Biochemistry and Genetics, Center for Biomolecular Recognition, Biochemistry Laboratory B, The Panum Institute, Copenhagen, 2200, Den.
SO Advanced Drug Delivery Reviews (2003), 55(2), 267-280 CODEN: ADDREP; ISSN: 0169-409X
PB Elsevier Science B.V.
DT Journal; General Review
LA English
AB A review. ***Peptide*** ***nucleic*** ***acid*** (***PNA***) is a DNA mimic having a pseudopeptide backbone that makes it extremely stable in biol. fluids. ***PNA*** binds complementary RNA and DNA with high affinity and specificity. These qualities make ***PNA*** a leading agent among third generation' ***antisense*** and antigene agents. Unfortunately, fast progress in the exploration of ***PNA*** as an exptl. and therapeutical regulator of gene expression has been hampered by the poor cellular uptake of ***PNA*** . However, a no. of transfection protocols for ***PNA*** have now been established. These include microinjection, electroporation, co-transfection with DNA, conjugation to lipophilic moieties, conjugation to peptides, etc. Here we give a short introduction to the basic findings on ***PNA*** as an ***antisense*** and antigene agent in cell-free in vitro systems. This is followed by a comprehensive evaluation of the most interesting literature concerning cellular delivery and the intracellular effect of ***PNA*** . Also the current progress as regards using ***PNA*** as co-factor in DNA delivery is reviewed.
RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 48 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:29496 CAPLUS
DN 138:85350
TI Designing ***peptide*** ***nucleic*** ***acid*** (***PNA***) sequences by determining the stability of ***PNA*** /DNA hybrid duplexes with binding energy calculation via nearest-neighbor base-pair modeling
IN Sudo, Yukio; Sugimoto, Naoki
PA Fuji Photo Film Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp. CODEN: JKXXAF

DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ----
---------- ---- -------- ---------- --------
PI JP 2003009876 A2 20030114 JP 2001-200370 20010702
PRAI JP 2001-200370 20010702
AB A new method for designing ***peptide*** ***nucleic*** ***acid*** (***PNA***) sequences by detg. the stability of ***PNA*** /DNA hybrid duplexes by calcg. the binding energy using the nearest-neighbor base-pair model, is disclosed. Designing of ***antisense*** nucleic acids, based on the method is claimed. Enthalpy change (.DELTA.H), entropy change (.DELTA.S), and free energy change (.DELTA.G), are calcd. The authors have examd. quant. stabilities of ***PNA*** /DNA hybrid duplexes with identical nearest-neighbor base pairs and compared stabilities between ***PNA*** /DNA. Energetic behaviors of eight pairs of ***PNA*** /DNA hybrid duplexes with identical nearest neighbors have been investigated by UV melting anal. In the pairs with identical nearest-neighbor pairs, the melting curve traces at the same strand concn. were very similar. These results indicate that the nearest-neighbor model is valid for predicting the stability of ***PNA*** /DNA hybrid duplexes as well as ***PNA*** /RNA and DNA/DNA duplexes.

L9 ANSWER 49 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:11233 CAPLUS
DN 139:7147
TI Monofunctionally trans-diammine platinum(II)-modified ***peptide*** ***nucleic*** ***acid*** oligomers: a new generation of potential ***antisense*** drugs
AU Schmidt, Kathrin S.; Boudvillain, Marc; Schwartz, Annie; Van der Marel, Gijs A.; Van Boom, Jacques H.; Reedijk, Jan; Lippert, Bernhard
CS Fachbereich Chemie, Universitat Dortmund, Dortmund, 44227, Germany
SO Chemistry--A European Journal (2002), 8(24), 5566-5570 CODEN: CEUJED; ISSN: 0947-6539
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
OS CASREACT 139:7147
AB A solid-phase approach is described that provides facile access to monofunctionally trans-PtII-modified ***PNA*** oligomers of arbitrary sequence for potential use both in antigene and ***antisense*** strategies. The approach includes the synthesis of a platinated building block (I) and its subsequent incorporation into three different ***PNA*** oligomers by solid-phase synthesis. In a model crosslinking reaction one of the latter is found to recognize sequence-specifically a target oligonucleotide and to cross-link to it. The resulting structure is the trans-PtII-cross-linked ***PNA*** /DNA duplex as revealed by mass spectrometry in combination with a Maxam-Gilbert sequencing expt.
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 50 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:963489 CAPLUS
DN 139:129710
TI Caspase-3 colorimetric assay
AU Zeng, Lizhi; Smith, Larry D.
CS H.L. Snyder Medical Research Institute, Winfield, KS, 67156, USA
SO BioTechniques (2002), 33(6), 1196-1197 CODEN: BTNQDO; ISSN: 0736-6205
PB Eaton Publishing Co.
DT Journal
LA English
AB The ApoAlert caspase-3 colorimetric assay kit was used for murine bone marrow-derived mast cells and human Burkitt lymphoma cells with apoptosis induced by cytokine depletion and ***antisense*** p21 transfection, resp. A 3.3-fold or five-fold increase of caspase-3 activity was noted in the induced samples. A min. of three-fold increase in caspase-3 activity was obsd. after induction of Jurkat cell in which apoptosis was induced by 40 .mu.M actinomycin D for 15 h compared to uninduced controls. The ***pNA*** calibration curve generated with boiling was identical to the curve without boiling, suggesting that the ***pNA*** was stable at 100.degree.. Using the modified procedure for the kit, a seven-fold increase in caspase-3 activity was noted in induced against uninduced samples. These findings showed that arsenite-induced apoptosis of this cell line was through the activation of caspase-3.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 51 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:958280 CAPLUS
DN 138:249595
TI ***PNA*** Targeting the PBS and A-Loop Sequences of HIV-1 Genome Destabilizes Packaged tRNA3Lys in the Virions and Inhibits HIV-1 Replication
AU Kaushik, Neerja; Pandey, Virendra N.
CS Cent. Study Emerging Re-Emerging Pathogensk Dep. Biochem. Mol. Biol., UMD-New Jersey Med. Sch., Newark, NJ, 07103, USA
SO Virology (2002), 303(2), 297-308 CODEN: VIRLAX; ISSN: 0042-6822
PB Elsevier Science
DT Journal
LA English
AB During assembly of the HIV-1 virions, cellular tRNALys3 is packaged into the virion particles and is utilized as a primer for the initiation of reverse transcription. The 3'-terminal 18 nucleotides of the cellular tRNALys3 are complementary to nucleotides 183-201 of the viral RNA genome, referred to as the primer binding sequence (PBS). Addnl. sequences (A-Loop) upstream of the PBS are essential for tRNA primer selection. We report here that a ***PNA*** targeted to PBS and A-Loop sequence (PNAPBS) exhibits high specificity for its target sequence and prevents tRNALys3 priming on the viral genome. We also demonstrate that PNAPBS is able to invade the duplex region of the tRNALys3-viral RNA complex and destabilize the priming process, thereby inhibiting the in vitro initiation of reverse transcription. The endogenously packaged tRNALys3 bound to the PBS region of the viral RNA genome in the HIV-1 virion is efficiently competed out by PNAPBS, resulting in near complete inhibition of initiation of endogenous reverse transcription. Examn. of the effect of PNAPBS on HIV-1 prodn. in CEM cells infected with pseudotyped HIV-1 virions carrying luciferase reporter exhibited dramatic redn. of HIV-1 replication by nearly 99%. Anal. of the mechanism of PNAPBS-mediated inhibition indicated that PNAPBS interferes at the step of reverse transcription. These findings suggest the antiviral efficacy of PNAPBS in blocking the process of HIV-1 replication.
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 52 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:954799 CAPLUS
DN 138:250304
TI Aminoacylation of tRNA by ***antisense*** molecule

AU Ninomiya, Keiko; Endo, Takamasa; Minohata, Toshikazu; Tajiri, Masahisa; Suzuki, Maya; Kurita, Tomoyoshi; Hohsaka, Takahiro; Sisido, Masahiko
CS Department of Bioscience and Biotechnology, Faculty of Engineering, Okayama University, Okayama, 700-8530, Japan
SO Nucleic Acids Research Supplement (2002), 2(Twenty-ninth Symposium on Nucleic Acids Chemistry), 101-102 CODEN: NARSCE
PB Oxford University Press
DT Journal
LA English
AB Aminoacylation of tRNA was attempted through formation of tRNA/DNA/aa- ***PNA*** (N-aminoacylated ***peptide*** ***nucleic*** ***acid***) ternary hybrid. A 23-mer DNA, that is complementary to a 3'- terminal of tRNA and to a 9-mer ***PNA*** carrying an amino acid unit, was designed to achieve close proximity between the amino acid and the 3'-OH group of tRNA. The aminoacylation was carried out in a buffer soln. contg. imidazole. The aminoacylation was detected by nuclease S1 treatment followed by HPLC and MALDI-TOF MS. This novel methodol. will open a way for easy and versatile aminoacylation of nonnatural amino acids onto specific tRNAs.

L9 ANSWER 53 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:951094 CAPLUS
DN 138:399109
TI Down-regulation of amyloid precursor protein by ***peptide*** ***nucleic*** ***acid*** oligomer in cultured rat primary neurons and astrocytes
AU Adlerz, Linda; Soomets, Ursel; Holmlund, Linda; Viirlaid, Sade; Langel, Ulo; Iverfeldt, Kerstin
CS Department of Neurochemistry and Neurotoxicology, Stockholm University, Stockholm, SE-10691, Swed.
SO Neuroscience Letters (2003), 336(1), 55-59 CODEN: NELED5; ISSN: 0304-3940
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB The amyloid precursor protein (APP) and its proteolytic cleavage products, the amyloid .beta. peptides, have been implicated as a cause of Alzheimer's disease. Peptide nucleic acids (***PNA***), the DNA mimics, have been shown to block the expression of specific proteins at both transcriptional and translational levels. Generally, the cellular uptake of ***PNA*** is low. However, recent studies have indicated that the effect of unmodified ***antisense*** ***PNA*** uptake is more pronounced in nervous tissue. In this study we have shown that biotinylated ***PNA*** directed to the initiator codon region of the APP mRNA (-4 - +11) was taken up into the cytoplasm of primary rat cerebellar granule cells and cortical astrocytes, using fluorescence and confocal microscopy studies. Uptake of ***PNA*** was faster in neurons than in astrocytes. Western blotting anal. showed that APP was strongly down-regulated in both neurons and astrocytes. Thus, unmodified ***PNA*** can be used for studies on the function of APP in neurons and astrocytes.
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 54 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:921890 CAPLUS
DN 138:19496
TI ***Antisense*** compositions targeted to .beta.1-adrenoceptor-specific mRNA for treatment of cardiovascular disorders
IN Phillips, M. Ian; Zhang, Yuan
PA University of Florida, USA
SO U.S., 103 pp., Cont.-in-part of WO 2000 15,783. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI US 6489307 B1 20021203 US 2000-614034 20000711 US 6087343 A 20000711 US 1998-152717 19980914 WO 2000015783 A2 20000323 WO 1999-US21007 19990914 WO 2000015783 A3 20000720 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG WO 2002004623 A2 20020117 WO 2001-US21759 20010711 WO 2002004623 A3 20021227 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1301593 A2 20030416 EP 2001-955810 20010711 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR US 2003191080 A1 20031009 US 2002-308503 20021203
PRAI US 1998-152717 A2 19980914 WO 1999-US21007 A2 19990914 US 2000-614034 A 20000711 WO 2001-US21759 W 20010711
AB Disclosed are ***antisense*** oligonucleotide, polynucleotide, and ***peptide*** ***nucleic*** ***acid*** compds. that specifically bind to mammalian mRNA encoding a .beta.1-adrenoceptor polypeptide and that are useful in the control and/or treatment of cardiac dysfunction, hypertension, hypertrophy, myocardial ischemia, and other cardiovascular diseases in an affected mammal, and preferably, in a human subject. The ***antisense*** compds. disclosed herein, and pharmaceutical formulations thereof, provide sustained control of .beta.1-adrenoceptor expression over prolonged periods, and achieve therapeutic effects from as little as a single dose. Administration of these ***antisense*** compns. to approved animal models resulted in a decrease in blood pressure, but no significant change in heart rate. Use of such ***antisense*** compns. in the redn. of .beta.1-adrenoceptor polypeptides in a host cell expressing .beta.1-adrenoceptor-specific mRNA, and in the prepn. of medicaments for treating human and animal diseases, and in particular, hypertension and other cardiac dysfunction is also disclosed.
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 55 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:906554 CAPLUS
DN 138:1044
TI G protein-coupled receptor (GPCR) microarrays for determination of GPCR gene expression profiles and uses in drug and toxin screening and diagnostics
IN Thirstrup, Kenneth; Madsen, Lars Siim; Jensen, Jens Bitsch; Hummel, Rene; Jensen, Bo Skaaning
PA Azign Bioscience A/s, Den.
SO PCT Int. Appl., 43 pp. CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ----
---------- ---- -------- ---------- --------
PI WO 2002095065 A2 20021128 WO 2002-DK337 20020521 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI DK 2001-802 A 20010518
AB The invention provides G protein-coupled receptor (GPCR) arrays, kits comprising GPCR arrays and methods to produce such GPCR arrays. GPCR arrays are useful in the detn. of GPCR expression profiles in biol. materials and also in the identification of therapeutic, prophylactic and/or toxic agents involved in the response of the GPCR expression. The invention relates to an GPCR array comprising a multiplicity of individual GPCR polynucleotide spots stably assocd. with a surface of a solid support, wherein an individual GPCR polynucleotide spot comprises an GPCR polynucleotide compn. comprising a non-conserved region of an GPCR polynucleotide family member, the spots representing at least two different regions of an GPCR polynucleotide member of a family. The invention also relates to a set of primers specific for nonconserved regions of GPCR polynucleotide family members, wherein the set of primers are used in the method for the prodn. of an array according to the invention. In still a further aspect, the invention relates to a diagnostic method to det. the differences of GPCR expression profiles between two different biol. materials.

L9 ANSWER 56 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:906553 CAPLUS
DN 138:1043
TI Transporter microarrays for the determination of transporter gene expression profiles and uses in drug and toxin screening and diagnostics
IN Jensen, Jens Bitsch; Madsen, Lars Siim; Gether, Ulrik; Jensen, Bo Skaaning
PA Azign Bioscience A/S, Den.
SO PCT Int. Appl., 41 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ----
---------- ---- -------- ---------- --------
PI WO 2002095064 A1 20021128 WO 2002-DK336 20020521 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI DK 2001-803 A 20010518
AB The object of the invention is to provide transporter arrays, kits comprising transporter arrays and methods to produce such transporter arrays. Transporter arrays are useful in the detn. of transporter expression profiles in biol. materials and also in the identification of therapeutic, prophylactic and/or toxic agents involved either directly or indirectly in the response of the transporter expression. The invention relates to an transporter array comprising a multiplicity of individual transporter polynucleotide spots stably assocd. with a surface of a solid support, wherein an individual transporter polynucleotide spot comprises an transporter polynucleotide compn. comprising a non-conserved region of an transporter polynucleotide family member, the spots representing at least two different regions of a transporter polynucleotide. A set of primers specific for nonconserved regions of transporter polynucleotide family members are provided, wherein the set of primers are used in the method for the prodn. of an array according to the invention. A diagnostic method detecting the differences of transporter expression profiles between two different biol. materials is also provided.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 57 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:898055 CAPLUS
DN 138:249569
TI Systemically delivered ***antisense*** oligomers upregulate gene expression in mouse tissues
AU Sazani, Peter; Gemignani, Federica; Kang, Shin-Hong; Maier, Martin A.; Manoharan, Muthiah; Persmark, Magnus; Bortner, Donna; Kole, Ryszard
CS Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC, 27599, USA
SO Nature Biotechnology (2002), 20(12), 1228-1233 CODEN: NABIF9; ISSN: 1087-0156
PB Nature Publishing Group
DT Journal
LA English
AB Systemically injected 2'-O-methoxyethyl (2'-O-MOE)-phosphorothioate and ***PNA*** -4K oligomers (***peptide*** ***nucleic*** ***acid*** with four lysines linked at the C terminus) exhibited sequence-specific ***antisense*** activity in a no. of mouse organs. Morpholino oligomers were less effective, whereas ***PNA*** oligomers with only one lysine (***PNA*** -1K) were completely inactive. The latter result indicates that the four-lysine tail is essential for the ***antisense*** activity of ***PNA*** oligomers in vivo. These results were obtained in a transgenic mouse model designed as a pos. readout test for activity, delivery, and distribution of ***antisense*** oligomers. In this model, the expressed gene (EGFP-654) encoding enhanced green fluorescence protein (EGFP) is interrupted by an aberrantly spliced mutated intron of the human .beta.-globin gene. Aberrant splicing of this intron prevented expression of EGFP-654 in all tissues, whereas in tissues and organs that took up a splice site-targeted ***antisense*** oligomer, correct splicing was restored and EGFP-654 expression upregulated. The sequence-specific ability of ***PNA*** -4K and the 2'-O-MOE oligomers to upregulate EGFP-654 provides strong evidence that systemically delivered, chem. modified oligonucleotides affect gene expression by sequence-specific true ***antisense*** activity, validating their application as potential therapeutics.
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 58 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:884305 CAPLUS
DN 138:120443
TI ***Antisense*** inhibition of gene expression in human dendritic cells by ***peptide*** ***nucleic*** ***acid*** against CD86
AU Feng, Gang; Li, Shengfu; Li, Youping; Bu, Hong; Yang, Yuru; Lu, Yiping

CS Lab of Transplant Engineering and Immunology, West China Hospital, Sichuan University, Chengdu, 610041, Peop. Rep. China
SO Huaxi Yike Daxue Xuebao (2002), 33(2), 192-195 CODEN: HYDXET; ISSN: 0257-7712
PB Huaxi Yike Daxue
DT Journal
LA Chinese
AB Dendritic cells (DCs) are the most potent antigen presenting cells (APCa) of the immune system. The blockage effects of ***antisense*** peptide nucleic acids, a novel synthetic structural DNA mimic, on the expression of CD86 in DCs and the second signal transmission were studied. Human DCs grown up from peripheral blood monocytes in granulocyte-macrophage colony-stimulating factor (GM-CSF) and interleukin-4 (IL-4) were collected. ***Antisense*** ***PNA*** internalization was obsd. by laser scan confocal microscope (LSCM), and expression of CD86 protein and mRNA in DCs was detd. by fluorescence immunocytochem., flow cytometry, and RT-PCR. LSCM showed that the cultured immature DCs could internalized ***PNA*** efficiently. ***Antisense*** ***PNA*** DC exhibited striking redns. in cell surface staining for CD86, but not MHC class II, and were poor stimulators of T cell proliferation. RT-PCR found that ***PNA*** depressed the amts. of CD86 mRNA in DCs. ***Antisense*** ***PNA*** against CD86 could inhibit the expression of CD86 mRNA and protein in DCs, and the blockade of B7/CD28 pathway may increase the potential of costimulatory mol.-deficient ***antisense*** ***PNA*** DCs of donor origin to induce long-lasting allograft survival.

L9 ANSWER 59 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:837521 CAPLUS
DN 138:52027
TI Radiometal-Labeled Peptide- ***PNA*** Conjugates for Targeting bcl-2 Expression: Preparation, Characterization, and in Vitro mRNA Binding
AU Lewis, Michael R.; Jia, Fang; Gallazzi, Fabio; Wang, Yi; Zhang, Jiuli; Shenoy, Nalini; Lever, Susan Z.; Hannink, Mark
CS Department of Veterinary Medicine and Surgery, Department of Radiology, Department of Chemistry, University of Missouri Research Reactor, Columbia, MO, 65211, USA
SO Bioconjugate Chemistry (2002), 13(6), 1176-1180 CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
AB A new ***antisense*** peptide- ***peptide*** ***nucleic*** ***acid*** (peptide- ***PNA***) conjugate, designed for targeting bcl-2 expression, has been radiolabeled, characterized, and evaluated for bcl-2 mRNA binding in a cell-free system. A ***PNA*** complementary to the first six codons of the bcl-2 gene was synthesized by std. solid-phase Fmoc chem. and conjugated to a new deriv. of 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA) that allows macrocyclic radiometal chelates to be incorporated into any sequence position of a peptide- ***PNA*** conjugate. The DOTA- ***PNA*** conjugate was then coupled to a membrane-permeating transduction peptide, PTD-4, designed for intracellular delivery of the radiolabeled ***PNA*** . The conjugate was characterized by HPLC and ESI-MS and labeled with 111In and 90Y to high specific activities (>1000 Ci/mmol) with high radiochem. purity. Northern blot anal. showed that 90Y-PTD-4-K(DOTA)-anti-bcl-2- ***PNA*** bound specifically to as little as 50 fmol of bcl-2 mRNA, a result equiv. to that obtained with the analogous 32P-labeled DNA ***antisense*** oligonucleotide. Thus, the mRNA targeting properties of 111In- and 90Y-PTD-4-K(DOTA)-anti-bcl-2- ***PNA*** demonstrate potential for diagnostic imaging and targeted radiotherapy applications in bcl-2-pos. cancers.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 60 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:836588 CAPLUS
DN 138:182625
TI Oncogene mRNA imaging with 99mTc-chelator- ***PNA*** -peptides
AU Wickstrom, E.; Tian, X.; Rao, P. S.; Thakur, M. L.; Qin, W.; Sauter, E. R.
CS Department of Microbiology and Immunology, Thomas Jefferson University, Philadelphia, PA, 19107, USA
SO Russian Chemical Bulletin (Translation of Izvestiya Akademii Nauk, Seriya Khimicheskaya) (2002), 51(7), 1083-1099 CODEN: RCBUEY; ISSN: 1066-5285
PB Kluwer Academic/Consultants Bureau
DT Journal
LA English
AB [99mTc] ***PNA*** -peptide conjugates capable of binding to IGF1 receptors will be synthesized. Specificity of their uptake and hybridization to mRNA in normal epithelial human cells compared to human breast cancer cells will be studied.
RE.CNT 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 61 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:832908 CAPLUS
DN 137:347474
TI Ion channel microarrays for the determination of ion channel gene expression profiles and uses in drug and toxin screening and diagnostics
IN Jensen, Bo Skaaning; Madsen, Lars Siim; Jensen, Jens Bitsch; Kjaer, Katrine
PA Neurosearch A/S, Den.
SO PCT Int. Appl., 53 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2002086050 A2 20021031 WO 2002-DK253 20020418 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI DK 2001-635 A 20010420
AB The invention provides completely novel and improved ion channel arrays, kits comprising ion channel arrays and methods to produce such ion channel arrays. Ion channel arrays are useful in the detn. of ion channel expression profiles in a certain biol. material, several biol. materials and also in the identification of therapeutic, prophylactic and/or toxic agents involved either directly or indirectly in the response of the ion channel expression. In a first aspect the invention relates to an ion channel array comprising a multiplicity of individual ion channel polynucleotide spots stably assocd. with a surface of a solid support, wherein an individual ion channel polynucleotide spot comprises an ion channel polynucleotide compn. comprising a non-conserved region of an ion channel polynucleotide family

member, the spots representing at least two different regions of an ion channel polynucleotide member of a family. In a further aspect, the invention relates to a set of primers specific for nonconserved regions of ion channel polynucleotide family members, wherein the set of primers are used in the method for the prodn. of an array according to the invention. In still a further aspect, the invention relates to a diagnostic method to det. the differences of ion channel expression profiles between two different biol. materials; said method comprises obtaining a first ion channel expression profile of a first biol. material according to the method of the present invention, obtaining a second ion channel expression profile of a second biol. material according to the method of the present invention, comparing the first and second ion channel expression profiles, and identifying any difference in the ion channel expression profile.

L9 ANSWER 62 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:805617 CAPLUS
DN 139:64923
TI (2'-O-methyl-RNA)-3'- ***PNA*** chimeras: A new class of mixed backbone oligonucleotide analogues with high binding affinity to RNA
AU Greiner, Beate; Breipohl, Gerhard; Uhlmann, Eugen
CS Aventis Pharma Deutschland GmbH, Frankfurt a.M., D-65926, Germany
SO Helvetica Chimica Acta (2002), 85(9), 2619-2626 CODEN: HCACAV; ISSN: 0018-019X
PB Verlag Helvetica Chimica Acta
DT Journal
LA English
OS CASREACT 139:64923
AB The automated online synthesis of DNA-3'- ***PNA*** chimeras 1-4 and (2'-O-methyl-RNA)-3'- ***PNA*** chimeras 5-8 is described, in which the 3'-terminal part of the oligonucleotide is linked to the N-terminal part of the ***PNA*** via N-(.omega.-hydroxyalkyl)-N-[(thymin-1- yl)acetyl]glycine units (alkyl=Et, Ph, Bu, and pentyl). By means of UV thermal denaturation, the binding affinities of all chimeras were directly compared by detg. their Tm values in the duplex with complementary DNA and RNA. All investigated DNA-3'- ***PNA*** chimeras and (2'-O-methyl-RNA)-3'- ***PNA*** chimeras form more-stable duplexes with complementary DNA and RNA than the corresponding unmodified DNA. Interestingly, a N-(3-hydroxypropyl)glycine linker resulted in the highest binding affinity for DNA-3'- ***PNA*** chimeras, whereas the (2'-O-methyl-RNA)-3'- ***PNA*** chimeras showed optimal binding with the homologous N-(4-hydroxybutyl)glycine linker. The duplexes of (2'-O-methyl-RNA)-3'- ***PNA*** chimeras and RNA were significantly more stable than those contg. the corresponding DNA-3'- ***PNA*** chimeras. Surprisingly, we found that the charged (2'-O-methyl-RNA)-3'- ***PNA*** chimera with a N-(4-hydroxybutyl)glycine-based unit at the junction to the ***PNA*** part shows the same binding affinity to RNA as uncharged ***PNA*** . Potential applications of (2'-O-methyl-RNA)-3'- ***PNA*** chimeras include their use as ***antisense*** agents acting by a RNase-independent mechanism of action, a prerequisite for ***antisense*** -oligonucleotide-mediated correction of aberrant splicing of pre-mRNA.
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 63 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:778171 CAPLUS
DN 137:289892
TI Antibiotic-free bacterial strain selection with ***antisense*** molecules against essential genes
IN Nielsen, Peter E.; Good, Liam
PA Kobenhavns Universitet, Den.
SO PCT Int. Appl., 92 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- --------------- --------
PI WO 2002079467 A2 20021010 WO 2002-DK208 20020326 W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI DK 2001-523 A 20010329
AB A new method for an antibiotic-free selection of genetically modified cells is described. It is shown that ***antisense*** mols. targeted to an essential gene inhibit growth may be used for growth selection of cells transformed with a plasmid carrying an altered version of the essential gene. The ***antisense*** mol. may be an ***antisense*** DNA or an ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***). The results show that ***antisense*** mols. may be used for antibiotic-free selection of desired transformed microbes when targeted against an essential microbial gene. This technol. is useful in genetic engineering for research growth and isolation of transformed organisms, and for industrial growth maintenance of transformed organisms, e.g. in the prodn. of genetically engineered proteins as an environmentally safer alternative to traditional selection methods based on antibiotics. ***Antisense*** peptide nucleic acids are included in the incubation medium in the same way as an antibiotic would be used. Preliminary optimization expts. used ***antisense*** ***PNA*** to the lacZ gene. These expts. found the optimum length range for effective inhibition of gene expression and the effects of potential carrier peptides on the bactericidal activity of the PNAs. Use of ***antisense*** ***PNA*** to the acyl-carrier protein gene acpP of Escherichia coli and of Bacillus subtilis as a selectable marker is demonstrated. The use of ***antisense*** ***PNA*** to inhibit expression of a reporter gene without adverse effects on the host.

L9 ANSWER 64 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:774962 CAPLUS
DN 138:338463
TI Phosphono-PNAs: Synthesis, properties and applications
AU Efimov, V. A.; Chakhmakhcheva, O. G.
CS Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Moscow, 117991, Russia
SO Collection Symposium Series (2002), 5(Chemistry of Nucleic Acid Components), 135-144 CODEN: CSYSFN
PB Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic
DT Journal
LA English
AB A symposium report. The synthesis of a set of DNA mimics representing phosphonate analogs of peptide nucleic acids (pPNAs), ***PNA*** -pPNA hetero-oligomers and HypNA-pPNA chimeras contg. ***PNA*** -like mols. on the base of trans-4-hydroxy-L-proline (HypNA) as well as novel phosphono-HypNA (pHypNA) mimics has been accomplished. The evaluation of their effectiveness in assays based on the hybridization technique in comparison with natural oligonucleotides and classical PNAs has shown a high potential of these mimics as sensor mols. for

nucleic acid based diagnostics, mol. probes for nucleic acids isolation and ***antisense*** reagents.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 65 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:757288 CAPLUS
DN 137:243119
TI Human glycoprotein MGC-24 13.31 and its cDNA and therapeutic use thereof
IN Mao, Yumin; Xie, Yi
PA Bode Gene Development Co., Ltd., Shanghai, Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 33 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI CN 1331114 A 20020116 CN 2000-116945 20000630 WO 2002020776 A1 20020314 WO 2001-CN1088 20010629 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 2002012052 A5 20020322 AU 2002-12052 20010629
PRAI CN 2000-116945 A 20000630 WO 2001-CN1088 W 20010629
AB The invention provides cDNA sequences of a novel human peanut agglutinin (***PNA***)-binding cell surface glycoprotein MGC-24 (sequence homolog) 13.31 (also called MGC24-13.31) cloned from human embryonic brain. The invention also relates to constructing the cloned gene expression vectors to prep. its recombinant protein using E. coli or eukaryotic cells. Methods of expressing and prepg. the above recombinant protein and its antibody are described. The mRNA expression profile in various normal or tumor cell lines and tissues is also provided. The invention further relates to applications of related gene or protein products for the treatment of related diseases, such as cancer, blood diseases, HIV infection, immune diseases and inflammation. Methods for screening for related analogs, agonists, inhibitors and antagonists to be used as therapeutic drugs are also described.

L9 ANSWER 66 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:694979 CAPLUS
DN 138:248372
TI Using peptide nucleic acids as gene-expression modifiers to reduce .beta.-amyloid levels
AU McMahon, Beth M.; Stewart, Jennifer; Fauq, Abdul; Younkin, Steven; Younkin, Linda; Richelson, Elliott
CS Departments of Neuroscience and Pharmacology, Mayo Clinic, Jacksonville, FL, 32224, USA
SO Journal of Molecular Neuroscience (2002), 19(1/2), 71-76
CODEN: JMNEES; ISSN: 0895-8696
PB Humana Press Inc.
DT Journal
LA English
AB The deposition of amyloid .beta. peptide (A.beta.) is an early and crit. aspect of Alzheimer's disease. A.beta. is formed by the cleavage of amyloid precursor protein (APP). Studies of familial forms of Alzheimer's disease indicate that elevated secretion of A.beta., particularly A.beta.(1-42), is likely to be an etiol. agent in the disease. A.beta.(1-42) is known to cause fibril formation and at elevated levels increases aggregation, which can lead to neuronal death. It has, therefore, been hypothesized that if the levels of A.beta., particularly A.beta.(1-42), could be reduced that onset of Alzheimer's disease could be slowed or possibly prevented. The authors, therefore, propose using PNAs (peptide nucleic acids) targeted to APP to decrease plasma and brain levels of A.beta.(1-40) and A.beta.(1-42). This research project is designed to expand upon the discovery in the authors lab. that systemic administration of ***antisense*** or antigene treatments utilizing peptide nucleic acids (PNAs) can be used to target and shut down proteins. ***Antisense*** strategies are methods of specifically targeting a particular protein by inhibiting translation by complementary binding to mRNA, while antigene methods inhibit transcription by complementary binding to DNA. For expts. involving ***antisense*** strategies, there are several advantages to using PNAs as opposed to the traditional oligonucleotide approaches. The authors initially preformed the authors studies in rats and identified a ***PNA*** sequence that was able to significantly reduce the levels of A.beta.(1-41) in rat brain compared to vehicle control rats. The authors have switched to mice so that the authors can prep. to perform the authors expts. in a transgenic animal model of Alzheimer's disease. The authors have, however, run into several tech. difficulties with using mice compared to rats. In spite of this, the authors have identified one ***PNA*** sequence that specifically lowers mouse brain A.beta.(1-40) A.beta.(1-42) by 37% and 47%, resp.
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 67 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:692220 CAPLUS
DN 138:130645
TI ***Antisense*** inhibition of bacterial gene expression and cell growth
AU Good, Liam
CS Center for Genomics and Bioinformatics, Karolinska Institute, Stockholm, Swed.
SO Methods in Molecular Biology (Totowa, NJ, United States) (2002), 208(Peptide Nucleic Acids), 237-248 CODEN: MMBIED; ISSN: 1064-3745
PB Humana Press Inc.
DT Journal
LA English
AB ***Peptide*** ***nucleic*** ***acid*** (***PNA***) has been developed and these greatly improve the prospects for therapeutic development. ***Antisense*** PNAs that inhibit bacterial genes, such as lacZ and acpP, was described. Relatively simple guidelines for designing ***antisense*** peptide nucleic acids (PNAs) and peptide-PNAs are provided. In addn., straightforward and inexpensive assays to assess the ***antisense*** effects on reporter and essential genes are described.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 68 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:692218 CAPLUS
DN 138:118081
TI Lipid-mediated introduction of peptide nucleic acids into cells
AU Braasch, Dwaine A.; Corey, David R.
CS Department of Pharmacology and Biochemistry, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, USA

SO Methods in Molecular Biology (Totowa, NJ, United States) (2002), 208(Peptide Nucleic Acids), 211-223 CODEN: MMBIED; ISSN: 1064-3745
PB Humana Press Inc.
DT Journal
LA English
AB Peptide oligonucleotides have been used as ***antisense*** agent to block gene expression or to alter RNA splicing. This report describes a method for the delivery of peptide nucleic acids (PNAs) into cells as ***PNA*** -DNA heteroduplexes complexed with cationic lipid.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 69 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:692205 CAPLUS
DN 138:380860
TI ***PNA*** technology
AU Nielsen, Peter E.
CS Center for Biomolecular Recognition, IMBG, Biochemistry B, The Panum Institute, University of Copenhagen, Copenhagen N, Den.
SO Methods in Molecular Biology (Totowa, NJ, United States) (2002), 208(Peptide Nucleic Acids), 3-26 CODEN: MMBIED; ISSN: 1064-3745
PB Humana Press Inc.
DT Journal; General Review
LA English
AB A review focuses on ***peptide*** ***nucleic*** ***acid*** (***PNA***) chem., cellular uptake, ***antisense*** applications, and antigene properties. The gene delivery, antimicrobial and antiviral properties of PNAs, and diagnostics applications of PNAs are described.
RE.CNT 106 THERE ARE 106 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 70 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:669329 CAPLUS
DN 138:147951
TI ***Antisense*** peptide nucleic acids conjugated to somatostatin analogs and targeted at the n-myc oncogene display enhanced cytotoxicity to human neuroblastoma IMR32 cells expressing somatostatin receptors
AU Sun, Lichun; Fuselier, Joseph A.; Murphy, William A.; Coy, David H.
CS Tulane Health Sciences Center, Peptide Research Laboratories, Department of Medicine, Tulane University School of Medicine, New Orleans, LA, 70112-2699, USA
SO Peptides (New York, NY, United States) (2002), 23(9), 1557-1565 CODEN: PPTDD5; ISSN: 0196-9781
PB Elsevier Science Inc.
DT Journal
LA English
AB ***Peptide*** ***nucleic*** ***acid*** (***PNA***) sequences are synthetic versions of naturally occurring oligonucleotides which display improved binding properties to DNA and RNA, but are still poorly internalized across cell membranes. In an effort to employ the rapid binding/internalization properties of somatostatin agonist analogs and the over-expression of somatostatin receptors on many types of tumor cells, PNAs complementary to target sites throughout 5'-UTR, translation start site and coding region of the n-myc oncogene were conjugated to a somatostatin analog (SSA) with retention of high somatostatin biol. potency. IMR32 cells, which over-express somatostatin receptor type 2 (SSTR2) and contain the n-myc oncogene, were treated with these ***PNA*** -SSA conjugates. The results show that ***PNA*** conjugates targeted to the 5'-UTR terminus and to regions at or close to the translation start site could effectively inhibit n-myc gene expression and cell growth, whereas the non-conjugate PNAs were without effect at similar doses. The most potent inhibition of cell growth was achieved with PNAs binding to the translation start site, but those complementary to the middle coding region or middle upstream site between 5'-UTR and translation start site displayed no inhibition of gene expression. These observations were extended to four other cell lines: GH3 cells which express SSTRs with the n-myc gene, SKNSH cells contg. a silent n-myc gene without SSTR2, HT-29 cells carrying the c-myc but no n-myc gene, and CHO-K1 cells lacking SSTR2 with n-myc gene. The results show that there was almost no effect on these four cell lines. Our study indicates that PNAs conjugated to SSA exhibited improved inhibition of gene expression possibly due to facilitated cellular uptake of the PNAs. These conjugates were mRNA sequence- and SSTR2-specific suggesting that many other genes assocd. with tumor growth could be targeted using this approach and that SSA could be a novel and effective transportation vector for the ***PNA*** ***antisense*** strategy.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 71 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:666646 CAPLUS
DN 138:362214
TI Antiproliferative effect in chronic myeloid leukaemia cells by ***antisense*** peptide nucleic acids
AU Rapozzi, Valentina; Burm, Brigitte E. A.; Cogoi, Susanna; van der Marel, Gijs A.; van Boom, Jacques H.; Quadrifoglio, Franco; Xodo, Luigi E.
CS School of Medicine, Department of Biomedical Sciences and Technologies, University of Udine, Udine, 33100, Italy
SO Nucleic Acids Research (2002), 30(17), 3712-3721 CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB ***Peptide*** ***nucleic*** ***acid*** (***PNA***) is a synthetic DNA analog that is resistant to nucleases and proteases and binds with exceptional affinity to RNA. Because of these properties ***PNA*** has the potential to become a powerful therapeutic agent to be used in vivo. Until now, however, the use of ***PNA*** in vivo has not been much investigated. Here, we have attempted to reduce the expression of the bcr/abl oncogene in chronic myeloid leukemia KYO-1 cells using a 13mer ***PNA*** sequence (asPNA) designed to hybridize to the b2a2 junction of bcr/abl mRNA. To enhance cellular uptake asPNA was covalently linked to the basic peptide VKRKKKP (NLS-asPNA). Moreover, to investigate the cellular uptake by confocal microscopy, both PNAs were linked by their N-terminus to fluorescein (FL). Studies of uptake, carried out at 4 and 37 on living KYO-1 cells stained with hexidium iodide, showed that both NLS-asPNA-FL and asPNA-FL were taken up by the cells, through a receptor-independent mechanism. The intracellular amt. of NLS-asPNA-FL was about two to three times higher than that of asPNA-FL. Using a semi-quant. RT- PCR technique we found that 10 .mu.M asPNA and NLS-asPNA reduced the level of b2a2 mRNA in KYO-1 cells to 20.+-.5% and 60.+-.10% of the control, resp. Western blot anal. showed that asPNA promoted a significant inhibition of p210BCR/ABL protein: residual protein measured in cells exposed for 48 h to asPNA was .apprx.35% of the control. Addnl., asPNA impaired cell growth to 50.+-.5% of the control and inhibited completion of the cell cycle. In summary, these results demonstrate that a ***PNA*** 13mer is taken up by KYO-1 cells and is capable of producing a significant and specific

down-regulation of the bcr/abl oncogene involved in leukemogenesis.
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 72 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:618032 CAPLUS
TI Development of peptide nucleic acids-aminoglycoside conjugates
AU Charles, Irudaya Samy; Arya, Dev P.
CS Department of Chemistry, Clemson University, Clemson, SC, 29634, USA
SO Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), MEDI-180 Publisher: American Chemical Society, Washington, D. C. CODEN: 69CZPZ
DT Conference; Meeting Abstract
LA English
AB Peptide nucleic acids are DNA analogs contg. 2-aminoethyl glycine linkages in place of normal phosphodiester backbone. They are non-ionic achiral mols. capable of site-specific binding to DNA as well as RNA and are not susceptible to hydrolytic (enzymic) cleavage. Due to their high affinity, high specificity, and high stability with DNA/RNA obsd. in the in vitro expts., ***PNA*** oligomers are strong candidates for effective antigene and ***antisense*** drug design. Our recent studies with aminoglycosides-in particular neomycin, which showed their effectiveness as DNA/RNA/hybrid stabilizing agents, prompted us to design ***PNA*** -aminoglycoside conjugates. Their synthesis and binding properties will be presented.

L9 ANSWER 73 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:614341 CAPLUS
TI Design and evaluation of amphipathic peptides as cellular delivery vehicles for ***antisense*** PNAs
AU Maier, Martin A.; Kadaba, Neena S.; Wancewicz, Ed; Lackey, Chantal; Siwkowski, Andy; Gaarde, Bill; Manoharan, Muthiah
CS Department of Medicinal Chemistry, Isis Pharmaceuticals, Carlsbad, CA, 92008, USA
SO Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), CARB-011 Publisher: American Chemical Society, Washington, D. C. CODEN: 69CZPZ
DT Conference; Meeting Abstract
LA English
AB A series of amphipathic peptides has been designed and screened for free uptake and cytotoxicity to identify promising sequence motifs for cellular delivery of ***antisense*** peptide nucleic acids (PNAs). Synthesis of the corresponding ***PNA*** -peptide conjugates is described and the correlation between the physicochem. properties of the peptides and ***PNA*** -peptide conjugates and their biol. activity is discussed.

L9 ANSWER 74 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:587460 CAPLUS
DN 138:67136
TI Artificial nucleic acids
AU Wada, Takehiko
CS Graduate School of Engineering, Osaka University, Japan
SO Kagaku Furontia (2002), 5(Seimei Kagaku no Nyu Sentoraru Doguma), 63-73 CODEN: KFAUA3
PB Kagaku Dojin
DT Journal; General Review
LA Japanese
AB A review. The designing and application of non-natural nucleic acid mols. were discussed. Topics on the peptide (or polyamide) nucleic acids (PNAs) and their derivs. were mainly focused. Application of the ***PNA*** -based artificial nucleic acids (PRNA: peptide RNA) as ***antisense*** mols. and stereo structure designing of such mols. by mimicking the RNA conformation were discussed. Physico-chem. natures of the PRNA and its chimeric derivs. with DNA and possible manipulation of the hybridization process of the artificial nucleic acids by modulating mols. such as boric acid were also discussed.

L9 ANSWER 75 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:586341 CAPLUS
DN 138:299849
TI Imaging gene expression in the brain in vivo in a transgenic mouse model of Huntington's disease with an ***antisense*** radiopharmaceutical and drug-targeting technology
AU Lee, Hwa Jeong; Boado, Ruben J.; Braasch, Dwaine A.; Corey, David R.; Pardridge, William M.
CS Department of Medicine, UCLA School of Medicine, Los Angeles, CA, USA
SO Journal of Nuclear Medicine (2002), 43(7), 948-956 CODEN: JNMEAQ; ISSN: 0161-5505
PB Society of Nuclear Medicine
DT Journal
LA English
AB Disease-specific genes of unknown function can be imaged in vivo with ***antisense*** radiopharmaceuticals, providing the transcellular, transport of these mols. is enabled with drug-targeting technol. The current studies describe the prodn. of 16-mer ***peptide*** ***nucleic*** ***acid*** (***PNA***) that is ***antisense*** around the methionine initiation codon of the huntingtin gene of Huntington's disease (HD). Methods: The ***PNA*** is biotinylated, which allows for rapid capture by a conjugate of streptavidin and the rat 8D3 monoclonal antibody (mAb) to the mouse transferrin receptor (TfR), and contains a tyrosine residue, which enables radiolabeling with 125I. The reformulated ***PNA*** ***antisense*** radiopharmaceutical that is conjugated to the 8D3 mAb is designated 125I-***PNA*** /8D3. This form of the ***PNA*** is able to access endogenous transferrin transport pathways at both the blood-brain barrier and the brain cell membrane and undergoes both import from the blood to the brain and export from the brain to the blood through the TfR. Results: The ability of the ***PNA*** to hybridize to the target huntingtin RNA, despite conjugation to the mAb, was shown both with cell-free translation assays and with RNase protection assays. The 125I- ***PNA*** /8D3 conjugate was administered i.v. to either littermate control mice or to R6/2 transgenic mice, which express the exon 1 of the human HD gene. The mice were sacrificed 6 h later for frozen sectioning of the brain and quant. autoradiog. The studies showed a 3-fold increase in sequestration of the 125I-***PNA*** /8D3 ***antisense*** radiopharmaceutical in the brains of the HD transgenic mice in vivo, consistent with the selective expression of the HD exon-1 mRNA in these animals. Conclusion: These results support the hypothesis that gene expression in vivo can be quantitated with ***antisense*** radiopharmaceuticals, providing these mols. are reformulated with drug-targeting technol. Drug targeting enables access of the ***antisense*** agent to endogenous transport pathways, which permits passage across the cellular barriers that sep. blood and intracellular compartments of target tissues.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 76 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:582168 CAPLUS
DN 138:67133
TI Peptide ribonucleic acids (PRNA). A novel strategy for active control of DNA recognition through Borate Ester Formation
AU Wada, Takehiko
CS Graduate School of Engineering, Osaka University, Japan

SO Kagaku Kogyo (2002), 53(6), 443-448 CODEN: KAKOAY; ISSN: 0451-2014
PB Kagaku Kogyosha
DT Journal; General Review
LA Japanese
AB A review. Strategies for gene expression regulation by exogenous application of the anti-gene mols. such as ***antisense*** mols., triplex-forming nucleic acid and minor groove binders were described. The stereo chem. of RNA conformation in the interaction with DNA in hybridization formation was discussed by focusing on the energetic preference of the anti- and syn-configurations in the nucleotides recognition. The effects of the formation of borate-adduct with cis-diols of the nucleotide carbohydrate on nucleotide conformation and hybridization process were discussed. The approach to design specific antigene mols. based on these structural information was described by focusing the topics regarding the use of PRNA (peptide RNA) oligomers.

L9 ANSWER 77 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:575220 CAPLUS
DN 137:121604
TI Serine protease MP493 cDNA cloned from human stomach cancer cell line, and structure based inhibitor design
IN Nakamura, Yusuke; Sugano, Sumio; Matsusue, Tomokazu; Okamoto, Atsushi; Okawa, Kazufumi
PA Mochida Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 163 pp. CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2002059295 A1 20020801 WO 2002-JP465 20020123 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI JP 2001-14963 A 20010123
AB CDNA coding for a novel serine protease MP493 cloned from human stomach cancer cell line, recombinant expression, computer-aided screening or designing of compds. regulating its activity by using a partial three dimensional model structure thereof, an ***antisense*** nucleic acid against the DNA, and an antibody specific to the above protein, are disclosed. Expression of the mp493 gene was obsd. in lung, pancreas, kidney, and placenta. Serine protease activity was confirmed with the recombinant protein expressed in E. coli and COS-1 cells. Cleavage of the substrate Bz-L-Arg- ***pNA*** .HCl was inhibited by the serine protease inhibitor PMSF.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 78 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:539867 CAPLUS
DN 137:59620
TI Methods and kits for imaging of gene expression in the brain using ***antisense*** peptide nucleic acids linked to targeting ligands
IN Pardridge, William M.; Boado, Ruben J.
PA The Regents of the University of California, USA
SO PCT Int. Appl., 85 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2002055736 A2 20020718 WO 2001-US46361 20011203 WO 2002055736 A3 20030925 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2003165853 A1 20030904 US 2001-5996 20011203
PRAI US 2000-250990P P 20001204
AB This invention provides imaging reagents for the detection of a gene or gene expression product (e.g. mRNA) in a brain cell in vivo. Preferred reagents comprise a detectable label attached to a first nucleic acid that specifically hybridizes to the gene or to a nucleic acid transcribed from the gene. The first nucleic acid is linked to a targeting ligand that is capable of binding a receptor on a cell comprising the blood brain barrier and crossing said blood brain barrier. ***Antisense*** radiopharmaceuticals could be used to image gene expression in the brain in vivo, should these polar mols. be made transportable through the blood-brain barrier. The present studies describe an ***antisense*** imaging agent comprised of an iodinated ***peptide*** ***nucleic*** ***acid*** (***PNA***) conjugated to a monoclonal antibody to the rat transferrin receptor by using avidin-biotin technol. The ***PNA*** was a 16-mer ***antisense*** to the sequence around the methionine initiation codon of the luciferase mRNA. C6 rat glioma cells were permanently transfected with a luciferase expression plasmid, and C6 exptl. brain tumors were developed in adult rats. The expression of the luciferase transgene in the tumors in vivo was confirmed by measurement of luciferase enzyme activity in the tumor ext. The [125I] ***PNA*** conjugate was injected i.v. in anesthetized animals with brain tumors; the animals were killed 2 h later for frozen sectioning of brain and film autoradiog. No image of the luciferase gene expression was obtained after the administration of either the unconjugated antiluciferase ***PNA*** or a ***PNA*** conjugate that was ***antisense*** to the mRNA of a viral transcript. In contrast, tumors were imaged in all rats administered the [125I] ***PNA*** that was ***antisense*** to the luciferase sequence and was conjugated to the targeting antibody. In another embodiment, gene expression in transgenic mouse model of Huntington's disease is imaged. In conclusion, these studies demonstrate gene expression in the brain in vivo can be imaged with ***antisense*** radiopharmaceuticals that are conjugated to a brain drug-targeting system.

L9 ANSWER 79 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:537290 CAPLUS
DN 137:258856
TI Structural preorganization of peptide nucleic acids: chiral cationic analogues with five- or six-membered ring structures
AU Kumar, Vaijayanti A.
CS Division of Organic Chemistry Synthesis, National Chemical Laboratory, Pune, 411 008, India
SO European Journal of Organic Chemistry (2002), (13), 2021-2032 CODEN: EJOCFK; ISSN: 1434-193X
PB Wiley-VCH Verlag GmbH
DT Journal; General Review
LA English

AB A review. The advent of aminoethylglycyl peptide nucleic acids, aegPNAs, as strong and specific DNA/RNA binding agents has triggered much research activity directed towards the development of ***PNA*** -based ***antisense*** /antigen therapeutics. These efforts have mainly been directed towards further refinement of aegPNA properties such as water soly., cellular uptake and discrimination between parallel and anti-parallel binding modes. Introduction of chirality and also of pos./neg. charges in the ***PNA*** backbone has met with some success in this direction. The conformational freedom in the nucleobase linker arm and in the backbone aminoethyl and glycyl segments in the aegPNA backbone were found to be causes of unfavorable entropic loss during complex formation. Suitable clamping in the aegPNA backbone may reduce entropic loss and help produce a conformation appropriate for max. enthalpic benefits from nucleobase recognition. Introduction of constraint by means of five- or six-membered ring structures in the aegPNA and their contributions to maintaining the balance between rigidity and flexibility in the backbone have shown interesting effects on the overall stability of ***PNA*** -DNA/RNA complexes. This review presents an account of the literature in this direction. The significant promise of our approach, which makes use of the naturally occurring trans-4-hydroxy-1-proline to arrive at different chirally pure cyclic ***PNA*** analogs, is presented in this review, together with the DNA binding properties of the compds.
RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 80 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:529814 CAPLUS
DN 137:346791
TI Peptide nucleic acids targeted to the mouse proNPFFA reveal an endogenous opioid tonus
AU Bonnard, Elisabeth; Mazarguil, Honore; Zajac, Jean-Marie
CS CNRS UMR 5089, Institut de Pharmacologie et de Biologie Structurale, Toulouse, 31077, Fr.
SO Peptides (New York, NY, United States) (2002), 23(6), 1107-1113 CODEN: PPTDD5; ISSN: 0196-9781
PB Elsevier Science Inc.
DT Journal
LA English
AB Pharmacol. studies have implicated the anti-opioid neuropeptide FF (NPFF) in the modulation of pain transmission. Since its physiol. role has not yet been fully elucidated, the present study examd. whether ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***) complementary to the NPFF precursor (proNPFFA) modified pain sensitivity. Mice received three i.p. injections (10 mg/kg) of ***antisense*** ***PNA*** (As-proNPFFA) over a period of 24 h. As-proNPFFA treatment significantly increased the basal tail withdrawal latency in the tail-flick test. This analgesia persisted during 2 days and was completely reversed by naloxone. Thus, ***antisense*** PNAs, by decreasing anti-opioid effects, revealed a basal endogenous opioid activity. Our results evidence a physiol. interplay between NPFF and opioid systems and further support the use of ***PNA*** as effective ***antisense*** agents, for studying gene function in vivo.
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 81 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:514913 CAPLUS
DN 137:73903
TI New applications of ***peptide*** ***nucleic*** ***acid*** (***PNA***)
AU Suzuki, Tohru
CS Mol. Genet. Res. Cent., Gifu Univ., Gifu, 501-1193, Japan
SO Baiosaiensu to Indasutori (2002), 60(6), 385-388 CODEN: BIDSE6; ISSN: 0914-8981
PB Baioindasutori Kyokai
DT Journal; General Review
LA Japanese
AB A review on characterization of ***peptide*** ***nucleic*** ***acid*** (***PNA***), PCR clamping by ***PNA*** , application of ***PNA*** -directed PCR clamping to sequence reaction, and use of ***PNA*** as ***antisense*** oligonucleotides.

L9 ANSWER 82 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:504752 CAPLUS
DN 137:59902
TI Sulfur-containing amphiphilic agents for the transfer of biologically active molecules into cells
IN Keil, Oliver
PA G.O.T. Therapeutics G.m.b.H., Germany
SO PCT Int. Appl., 22 pp. CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- -------------- --------
PI WO 2002051800 A2 20020704 WO 2001-DE4843 20011221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG DE 10064870 A1 20020711 DE 2000-10064870 20001227 EP 1345893 A2 20030924 EP 2001-990354 20011221 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI DE 2000-10064870 A 20001227 WO 2001-DE4843 W 20011221
OS MARPAT 137:59902
AB The invention relates to amphiphilic, cationic, sulfo-substituted phosphatidylethanolamine analogs and salts thereof, which can complex biopolymers such as DNA, RNA, oligonucleotides, ribozymes, proteins and peptides and introduce the above into eukaryotic cells. Particularly suitable are compds. derived from 1,2-dioleoyl-3-sn- phosphatidylethanolamine (DOPE) and in which the phosphate ester group of DOPE is replaced by an isosteric group CH2-SO-CH2 or CH2S(O)2-CH2. Thus, 3-[(3,4-dioleoyloxybutyl)sulfonyl]propyl-1-ammonium trifluoroacetate (sulfectin A) and 3-[(3,4-dioleoyloxybutyl)sulfinyl]propyl-1-ammonium trifluoroacetate (sulfectin B) were synthesized. In transfection expts. with IMR 90 and F98 cell lines, sulfectin B alone provided better transfection efficiencies than did com. amphiphiles such as lipofectin. In the case of HeLa cells, the sulfectin required DOPE to provide comparable or better transfection efficiency.

L9 ANSWER 83 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:481699 CAPLUS
DN 137:181616
TI Labelled oligonucleotides as radiopharmaceuticals: Pitfalls, problems and perspectives
AU Younes, Cheraz Khelifi; Boisgard, Raphael; Tavitian, Bertrand
CS Laboratoire d'imagerie de l'expression des genes, INSERM ERIT-M0103, CEA/DSV/SHFJ, Orsay, 91401, Fr.

SO Current Pharmaceutical Design (2002), 8(16), 1451-1466
CODEN: CPDEFP; ISSN: 1381-6128
PB Bentham Science Publishers
DT Journal; General Review
LA English
AB A review. The labeling of single-stranded oligonucleotides with a positron or single-photon emitter can result in valuable radiopharmaceuticals with promising applications for: (i) Imaging of specific mRNAs, i.e. visualization of the expression of specific genes in vivo (ii) Monitoring of ***antisense*** chemotherapy, i.e. measuring the efficiency of efforts to block the expression of specific genes; (iii) Gene radiotherapy, i.e. the targeting of radiation damage to specific DNA sequences in order to destroy tumors; (iv) Imaging of protein targets by the use of aptamer oligonucleotides, i.e. oligonucleotide ligands obtained by in vitro evolution of selection-amplification steps, or selected for their interaction with nucleic acid-binding proteins; (v) Pretargeting strategies based on the specificity of complementary sequence hybridization. Nevertheless, oligonucleotides are intrinsically poor pharmaceuticals because of their large size, low stability, poor membrane passage and a no. of undesirable and sometimes unpredictable side effects. As an alternative to the inherently unstable phosphodiester DNAs, chem. modified oligonucleotides such as phosphorothioate, methylphosphonate and ***peptide*** ***nucleic*** ***acid*** oligomers have been developed, and some are in clin. trials for the chemotherapy of several types of tumors. Imaging techniques could be useful in the development of such therapies. In addn., the potential of targeting virtually any disease or physiol. process. by changing only the sequence of the oligomer, could provide a means to identify serious diseases in a very early stage, and be a highly specific modality to diagnose and differentiate various cancers. This has stimulated efforts to develop such radiopharmaceuticals in many labs., and encouraging results have been reported using technetium-99m, indium-111, carbon-11, fluorine-18, bromine-76 and iodine-125 labeled oligonucleotides.
RE.CNT 177 THERE ARE 177 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 84 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:481446 CAPLUS
DN 138:684
TI An approach towards synthetic microorganism from bio-macromolecular chemistry
AU Sishido, Masahiko
CS Department of Engineering, Okayama University, Tsushima naka, Okayama-shi, 700-8530, Japan
SO Kobunshi (2002), 51(6), 438-441 CODEN: KOBUA3; ISSN: 0454-1138
PB Kobunshi Gakkai
DT Journal; General Review
LA Japanese
AB A review. A synthetic strategy to prep. tRNA mols. bearing nonnatural amino acid (Xaa) was described. Introduction of the four-base codon (CGGC) to mRNA and corresponding anticodon to the Xaa tRNA were then described as the method for incorporating the Xaa at desired position of the target proteins. The prodn. of such artificial proteins in cell free translation system was presented with an actual example of streptavidin derivs. modified with coumaryl, nitrophenyl and/or anthranil-moieties. Instead of chem. synthesis, the use of ribozymes and engineered amino acyl-tRNA synthetase in the process of Xaa-tRNA prepn. were discussed. Application of the ***PNA*** mols. to design more efficient structures for sense- ***antisense*** recognition was also discussed.

L9 ANSWER 85 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:476601 CAPLUS
DN 138:145
TI Depletion of Bcl-2 by an ***antisense*** oligonucleotide induces apoptosis accompanied by oxidation and externalization of phosphatidylserine in NCI-H226 lung carcinoma cells
AU Koty, Patrick P.; Tyurina, Yulia Y.; Tyurin, Vladimir A.; Liu, Shang-Xi; Kagan, Valerian E.
CS Graduate School of Public Health, Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, USA
SO Molecular and Cellular Biochemistry (2002), 234/235(1&2), 125-133 CODEN: MCBIB8; ISSN: 0300-8177
PB Kluwer Academic Publishers
DT Journal
LA English
AB Oxidant-induced apoptosis involves oxidn. of many different and essential mols. including phospholipids. As a result of this non-specific oxidn., any signaling role of a particular phospholipid-class of mols. is difficult to elucidate. To det. whether preferential oxidn. of phosphatidylserine (PS) is an early event in apoptotic signaling related to PS externalization and is independent of direct oxidant exposure, the authors chose a genetic-based induction of apoptosis. Apoptosis was induced in the lung cancer cell line NCI-H226 by decreasing the amt. of Bcl-2 protein expression by preventing the translation of bcl-2 mRNA using an ***antisense*** bcl-2 oligonucleotide. Peroxidn. of phospholipids was assayed using a fluorescent technique based on metabolic integration of an oxidn.-sensitive and fluorescent fatty acid, cis-parinaric acid (***PnA***), into cellular phospholipids and subsequent HPLC sepn. of cis- ***PnA*** -labeled phospholipids. The authors found a decrease in Bcl-2 was assocd. with a selective oxidn. of PS in a sub-population of the cells with externalized PS. No significant difference in oxidn. of cis- ***PnA*** -labeled phospholipids was obsd. in cells treated with medium alone or a nonsense oligonucleotide. Treatment with either nonsense or ***antisense*** bcl-2 oligonucleotides was not assocd. with changes in the pattern of individual phospholipid classes as detd. by HPTLC. These metabolic and topog. changes in PS arrangement in plasma membrane appear to be early responses to ***antisense*** bcl-2 exposure that trigger a PS-dependent apoptotic signaling pathway. This obsd. externalization of PS may facilitate the 'labeling' of apoptotic cells for recognition by macrophage scavenger receptors and subsequent phagocytic clearance.
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 86 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:474121 CAPLUS
DN 138:133245
TI DNA-drug interactions
AU Ardhammar, Malin; Norden, Bengt; Kurucsev, Tomas
CS Department of Physical Chemistry, Chalmers University of Technology, Goteborg, Swed.
SO Circular Dichroism (2nd Edition) (2000), 741-768. Editor(s): Berova, Nina; Nakanishi, Koji; Woody, Robert W. Publisher: Wiley-VCH, New York, N. Y. CODEN: 69CTME; ISBN: 0-471-33003-5
DT Conference; General Review
LA English
AB A review on the use of CD (CD), particularly induced CD (ICD), to distinguish between the main types of DNA-dye binding geometries, i.e., intercalation and major- or minor-groove bindings. The details of the orientation and location of the ligand within its binding site as well as the occurrence of ligands bound in dimeric forms are discussed. The recently developed lead

compd. for ***antisense*** and antigene therapy, ***peptide*** ***nucleic*** ***acid*** (***PNA***) and its complexes with DNA, RNA and itself are also briefly described.
RE.CNT 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 87 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:429077 CAPLUS
DN 137:16555
TI Polynucleotides (cDNA and DNA), and polyproteins of human genes CAN-1, STG and SEEK-1, sequences, antibodies, and biological and/or diagnostic uses thereof, including use in diagnosing susceptibility to psoriasis
IN Charmley, Patrick; Moss, Patrick; McEuen, Mark
PA Celltech R & D, Inc., USA
SO PCT Int. Appl., 95 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2002044375 A2 20020606 WO 2001-US44506 20011127 WO 2002044375 A3 20030619 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2002115148 A1 20020822 US 2001-994365 20011126 AU 2002017915 A5 20020611 AU 2002-17915 20011127 EP 1343892 A2 20030917 EP 2001-998636 20011127 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2000-253592P P 20001128 US 2000-256839P P 20001215 WO 2001-US44506 W 20011127
AB The invention provides cDNA and genomic DNA mols. encoding human gene CAN-1 and STG proteins. The invention also provides: (1) information on single nucleotide polymorphism sites in genes CAN-1 and STG found in normal and psoriatic individuals; and (2) oligonucleotides that hybridize to cDNA and/or genomic DNA sequences of human STG and CAN-1 genes, or complements thereof. The invention further provides expression vectors contg. said human CAN-1 and STG nucleic acid mols., and use of said vectors in recombinant prodn. of gene CAN-1 and STG proteins. Still further, the invention provides: (1) isolated human proteins encoded by genes CAN-1, STG and SEEK-1; (2) antibodies specific for said proteins; (3) amino acid sequences of said proteins; (4) use of CAN-1, STG and SEEK-1 proteins in diagnosing susceptibility to psoriasis in an individual; and (5) method for ameliorating symptoms and/or progress of psoriasis by administering to patient a selective inhibitor of CAN-1, STG or SEEK-1 proteins. Finally, the invention provides a method for identifying a binding partner of human CAN-1, STG and SEEK-1 proteins, and use of identified CAN-1-binding partner in inhibiting movement of cells, hyperproliferation of keratinocytes, and abnormal differentiation of keratinocytes. The cDNA and genomic DNA sequences encoding human gene CAN-1 and STG proteins are disclosed. The invention related that a binding partner could be a macromol. selected from the following group: antibody, ***peptide*** , ***nucleic*** ***acid*** mol., steroid or steroid analog, or small org. mol. The invention related that said selective inhibitor could be an ***antisense*** oligonucleotide specific for mRNA of genes CAN-1, STG or SEEK-1. In the example section, the invention reported that genes CAN-1, STG and SEEK-1 map on chromosome 6 near the HLA C locus, and are expressed in skin and keratinocytes, and thus are candidate genes for involvement in genetic susceptibility towards psoriasis.

L9 ANSWER 88 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:424605 CAPLUS
DN 137:159196
TI Inhibition of Macrophage iNOS by Selective Targeting of ***Antisense*** ***PNA***
AU Chiarantini, Laura; Cerasi, Aurora; Fraternale, Alessandra; Andreoni, Francesca; Scari, Sonia; Giovine, Marco; Clavarino, Emanuela; Magnani, Mauro
CS Institute of Biochemistry "Giorgio Fornaini", Universita degli Studi di Urbino, Italy
SO Biochemistry (2002), 41(26), 8471-8477 CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB Peptide nucleic acids (PNAs) are synthetic polynucleobases that bind to DNA and RNA with high affinity and specificity and with poor membrane permeability. Although PNAs have an enormous potential as ***antisense*** agents, the success of ***antisense*** ***PNA*** applications will require efficient cellular uptake. In this study, a unique ***antisense*** 14-mer anti-inducible nitric oxide synthase (iNOS) was encapsulated into erythrocytes (RBC) by hypotonic dialysis. RBC loaded with ***PNA*** (10.5 .+-. 3.5 .mu.mol/mL RBC) were targeted specifically to murine macrophages, taking advantage of an in vitro opsonization induced by ZnCl2 and bis-sulfosuccynimidil-suberate (BS3). This in vitro opsonization enhanced the phagocytosis of loaded RBC and the delivery of ***PNA*** into macrophages (0.72 pmol/106 macrophages). The efficacy of this delivery system is demonstrated by decreases in NO prodn. and iNOS protein expression inside the macrophage. Therefore, we can suggest this novel approach for biomedical application.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 89 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:402787 CAPLUS
DN 137:273046
TI Peptide nucleic acids specifically cause antigene effects in vivo by systemic injection
AU McMahon, Beth M.; Stewart, Jennifer A.; Bitner, M. D.; Fauq, Abdul; McCormick, Daniel J.; Richelson, Elliott
CS Laboratory of Neuropsychopharmacology, Mayo Foundation for Medical and Educational Research, Jacksonville, FL, 32224, USA
SO Life Sciences (2002), 71(3), 325-337 CODEN: LIFSAK; ISSN: 0024-3205
PB Elsevier Science Inc.
DT Journal
LA English
AB Peptide nucleic acids (PNAs) are uncharged DNA analogs that hybridize to complementary sequences with high affinity and stability. We previously showed that PNAs, after i.p. injection into rats, are effective ***antisense*** compds. in vivo. The present study was designed to test whether PNAs also have antigene effects in vivo. The renin-angiotensin system is crit. in the control of blood pressure. We designed and synthesized sense (antigene) PNAs to angiotensinogen, which is the precursor protein that leads to angiotensin I and II. Spontaneously hypertensive rats received i.p. injections of either 20 mg/kg sense-angiotensinogen- ***PNA*** , mismatch-angiotensinogen ***PNA*** , or saline. Only the sense-angiotensinogen

PNA treatment resulted in a significant decrease in plasma angiotensin I, systolic blood pressure, and liver and brain angiotensinogen mRNA levels. Thus, these results demonstrate on the mol., protein, and physiol. levels that antigene PNAs are effective in vivo upon systemic administration.
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 90 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:394988 CAPLUS
DN 137:362908
TI Anticonvulsant activity of a nonpeptide galanin receptor agonist
AU Saar, Kulliki; Mazarati, Andrey M.; Mahlapuu, Riina; Hallnemo, Gerd; Soomets, Ursel; Kilk, Kalle; Hellberg, Sven; Pooga, Margus; Tolf, Bo-Ragnar; Shi, Tiejun S.; Hokfelt, Tomas; Wasterlain, Claude; Bartfai, Tamas; Langel, Ulo
CS Department of Neurochemistry and Neurotoxicology, Stockholm University, Stockholm, SE-10691, Swed.
SO Proceedings of the National Academy of Sciences of the United States of America (2002), 99(10), 7136-7141 CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Galanin is a neuropeptide with a wide variety of biol. functions, including that of a strong endogenous anticonvulsant. No nonpeptide ligands, capable of activating galanin receptors, are available today. Based on known pharmacophores of galanin, a combinatorial library was designed, synthesized, and screened at the rat hippocampal galanin receptor. A low mol. wt. galanin receptor agonist, 7-((9-fluorenylmethoxycarbonyl)cyclohexylalanyllysyl)amino-4-methylcoumarin (galnon) was found to displace 125I-galanin with micromolar affinity at Bowes cellular and rat hippocampal membranes. Autoradiog. binding assay on rat spinal cord sections confirmed the ability of galnon to displace 125I-galanin from its binding sites. Galnon inhibited adenylate cyclase activity, suggesting an agonist action at galanin receptors. When injected i.p. galnon reduced the severity and increased the latency of pentylenetetrazole-induced seizures in mice and reversed the proconvulsant effects of the galanin receptor antagonist M35, injected into a lateral ventricle. Intrahippocampal injection of galnon also shortened the duration of self-sustaining status epilepticus in rats, confirming its agonist properties in vivo. Pretreatment of rats with ***antisense*** ***peptide*** ***nucleic*** ***acid*** targeted to galanin receptor type 1 mRNA abolished the effect of galnon, suggesting mediation of its anticonvulsant properties through this receptor subtype. These findings introduce a systemically active nonpeptide galanin agonist anticonvulsant.
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 91 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:392187 CAPLUS
DN 136:396950
TI Direct, externally imposed control of nucleic acids
IN Jacobson, Joseph M.; Schwartz, John J.; Hamad, Kimberly; Zhang, Shuguang
PA USA
SO U.S. Pat. Appl. Publ., 18 pp. CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI US 2002061588 A1 20020523 US 2001-905832 20010713 US 2002119572 A1 20020829 US 2001-905831 20010713
PRAI US 2000-218312P P 20000714 US 2001-276388P P 20010316 US 2001-276313P P 20010316
AB Methods and compns. for rendering nucleic acids directly responsive to an external signal utilizing modulators that themselves respond to the external signal and are assocd. with the nucleic acid. In response to the external signal, the modulator alters phys. properties of the specific nucleic acid mol.(s) with which it is assocd., thereby altering the structural and functional properties thereof. The modulator may, for example, transfer applied energy to a nucleic acid, or to a portion of the nucleic acid, thereby changing the nucleic acid structure. The invention is useful in the nucleic acid hybridization techniques and applicable in in vivo transcription regulation.

L9 ANSWER 92 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:366119 CAPLUS
DN 138:106949
TI Accelerating RNA decay through intervention of RNAse L: Alternative synthesis of composite 2',5'-oligoadenylate-***antisense***
AU Torrence, Paul F.; Wang, Zhengfu
CS Department of Chemistry, Northern Arizona University, Flagstaff, AZ, 86011, USA
SO Methods in Enzymology (2001), 342(Ribonucleases, Part B), 20-28 CODEN: MENZAU; ISSN: 0076-6879
PB Academic Press
DT Journal; General Review
LA English
AB A review. An alternative method is outlined for the prepn. of 2-5A- ***peptide*** ***nucleic*** ***acid*** (***PNA***) ***antisense*** constructs which employs a convergent synthetic scheme, wherein the ***PNA*** and 2-5A are prepd. sep. and then linked in a final step. (c) 2001 Academic Press.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 93 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:332204 CAPLUS
DN 136:345809
TI Mucin-comprising vehicle for the transport of biologically-active agents
IN Shukla, Ashok Kumar; Shukla, Mukta M.; Shukla, Amita M.
PA USA
SO PCT Int. Appl., 33 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2002034763 A2 20020502 WO 2001-US50152 20011026 WO 2002034763 A3 20021010 W: JP RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR US 6320030 B1 20011120 US 2000-696897 20001026 US 2002090721 A1 20020711 US 2001-754868 20010105 US 2002099005 A1 20020725 US 2001-767462 20010123
PRAI US 2000-696897 A 20001026 US 2001-754868 A 20010105 US 2001-767462 A 20010123
AB A vehicle for the transport of biol. active or therapeutic agents into organisms, such as human beings, comprising mucin is described. The mucin component of the vehicle serves to enhance the transport of biol. active agents, such as therapeutic agents into living organisms; to control and/or improve the delivery of biol. active agents to cells, tissues, organs or organelles; to increase the level of specificity in targeting particular cells or cells types; and/or, to enhance the activity of such therapeutic agents once they enter an organism. The

vehicle described in the present invention is used to carry and deliver biol. active agents and can be used for biochem., therapeutic, clin., or other applications in organisms and cells including, but not limited to, delivery of DNA, RNA, ***PNA*** , polynucleotides and proteins into cells, tissues or organisms; gene delivery applications; in vivo gene therapy, ex vivo gene therapy or in vitro gene therapy; customized therapeutics; vaccination of organisms; genetic vaccination of organisms; and delivery of pharmaceutical products or biol. active chem., biochem. or biol. agents into cells and organisms.

L9 ANSWER 94 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:220635 CAPLUS
DN 136:259221
TI Novel phosphodiesterases of trypanosomes and human with potential use as therapeutic targets and cDNAs encoding
IN Beavo, Joseph A.; Seebeck, Thomas; Soderling, Scott Haydn; Rascon, Ana; Zoraghi, Roya; Kunz, Stefan; Gong, Kewei; Glavas, Natalie
PA USA
SO PCT Int. Appl., 165 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2002022661 A2 20020321 WO 2001-US28503 20010912
WO 2002022661 A3 20030313 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 2001089034 A5 20020326 AU 2001-89034 20010912 EP 1317553 A2 20030611 EP 2001-968819 20010912 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2000-232445P P 20000912 US 2000-240500P P 20001012 WO 2001-US28503 W 20010912
AB The present invention provides isolated full-length nucleic acid mols. encoding the novel cyclic nucleotide phosphodiesterases, and methods for uses thereof. The nucleic acid mols. of the invention also include peptide nucleic acids (***PNA***), and ***antisense*** mols. that react with the nucleic acid mols. of the invention. The invention also relates to agonists, antibodies, antagonists or inhibitors of the activity of novel PDE proteins. These compns. are useful for the diagnosis, prevention or treatment of conditions assocd. with the presence or the deficiency of novel PDE proteins. Characterization of the roles of the human cyclic nucleotide phosphodiesterases in T cell activation is reported. The Trypanosoma brucei genes were identified by searching sequence databases for sequences encoding the GAF and catalytic domains. Candidate sequence were cloned by PCR using sequence information from the search to design primers. Sequences complementing a phosphodiesterase deficient mutant of Saccharomyces cerevisiae were found.

L9 ANSWER 95 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:209592 CAPLUS
DN 137:89853
TI Cell permeabilization and uptake of ***antisense*** peptide-***peptide*** ***nucleic*** ***acid*** (***PNA***) into Escherichia coli
AU Eriksson, Magdalena; Nielsen, Peter E.; Good, Liam
CS Department of Physical Chemistry, Chalmers University of Technology, Goeteborg, SE-41296, Swed.
SO Journal of Biological Chemistry (2002), 277(9), 7144-7147 CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB ***Peptide*** ***nucleic*** ***acid*** (***PNA***) is a DNA mimic with promising properties for the development of ***antisense*** agents. ***Antisense*** PNAs targeted to Escherichia coli genes can specifically inhibit gene expression, and attachment of ***PNA*** to the cell-permeabilizing peptide KFFKFFKFFK dramatically improves ***antisense*** potency. The improved potency obsd. earlier was suggested to be due to better cell uptake; however, the uptake kinetics of std. or modified PNAs into bacteria had not been investigated. Here we monitored outer and inner membrane permeabilization by using chem. probes that normally are excluded from cells but can gain access at points where membrane integrity is disturbed. Membrane permeabilization was much more rapid in the presence of peptide- ***PNA*** conjugates relative to the free components used alone or in combination. Indeed, peptide-PNAs permeabilized E. coli nearly as quickly as antimicrobial peptides. Furthermore, as expected for outer membrane-active compds., added MgCl2 reduced cell-permeabilization. Concurrent monitoring of outer and inner membrane permeabilization indicated that passage across the outer membrane is rate-limiting for uptake. The enhanced cell-permeation properties of peptide-PNAs can explain their potent ***antisense*** activity, and the results indicate an unanticipated synergy between the peptide and ***PNA*** components.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 96 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:172575 CAPLUS
DN 136:194749
TI Novel ***Antisense*** and ***Peptide*** ***Nucleic*** ***Acid*** Strategies for Controlling Gene Expression
AU Braasch, Dwaine A.; Corey, David R.
CS Departments of Biochemistry and Pharmacology, University of Texas Southwestern Medical Center, Dallas, TX, 75390-9041, USA
SO Biochemistry (2002), 41(14), 4503-4510 CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal; General Review
LA English
AB A review that first describes the chem. and biol. properties of oligonucleotides and oligonucleotide mimics that contribute to the potency and specificity of ***antisense*** oligomers. The review then summarizes the substantial recent progress in the application of ***antisense*** and antigene oligomers for functional genomics and drug development. The review concludes by describing several novel strategies for using oligonucleotides to control gene expression. ***Antisense*** oligonucleotides have the potential to make revolutionary contributions to basic science and medicine. Oligonucleotides can bind mRNA and inhibit translation. Because they can be rapidly synthesized to be complementary to any sequence, they offer ideal tools for exploiting the massive amt. of genome information now available. However, until recently, this potential was largely theor., and ***antisense*** expts. often produced inconclusive or misleading outcomes. Oligomers with improved chem. properties, combined with advances in cell biol. and success in clin. trials, are affording powerful new options for basic research, biotechnol., and medicine.

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 97 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:164082 CAPLUS
DN 136:351931
TI Non-Watson-Crick interactions between ***PNA*** and DNA inhibit the ATPase activity of bacteriophage T4 Dda helicase
AU Tackett, Alan J.; Corey, David R.; Raney, Kevin D.
CS Department of Biochemistry and Molecular Biology, University of Arkansas for Medical Sciences, Little Rock, AR, 72205, USA
SO Nucleic Acids Research (2002), 30(4), 950-957 CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB ***Peptide*** ***nucleic*** ***acid*** (***PNA***) is a DNA mimic in which the nucleobases are linked by an N-(2-aminoethyl) glycine backbone. Here we report that ***PNA*** can interact with single-stranded DNA (ssDNA) in a non-sequence-specific fashion. We obsd. that a 15mer ***PNA*** inhibited the ssDNA-stimulated ATPase activity of a bacteriophage T4 helicase, Dda. Surprisingly, when a fluorescein-labeled 15mer ***PNA*** was used in binding studies, no interaction was obsd. between ***PNA*** and Dda. However, fluorescence polarization did reveal non-sequence-specific interactions between ***PNA*** and ssDNA. Thus, the inhibition of ATPase activity of Dda appears to result from depletion of the available ssDNA due to non-Watson-Crick binding of ***PNA*** to ssDNA. Inhibition of the ssDNA-stimulated ATPase activity was obsd. for several PNAs of varying length and sequence. To study the basis for this phenomenon, we examd. self-aggregation by PNAs. The 15mer ***PNA*** readily self-aggregates to the point of pptn. Since PNAs are hydrophobic, they aggregate more than DNA or RNA, making the study of this phenomenon essential for understanding the properties of ***PNA*** . Non-sequence-specific interactions between ***PNA*** and ssDNA were obsd. at moderate concns. of ***PNA*** , suggesting that such interactions should be considered for ***antisense*** and antigen applications.
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 98 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:159623 CAPLUS
DN 136:363633
TI Design of a Targeted ***Peptide*** ***Nucleic*** ***Acid*** Prodrug To Inhibit Hepatic Human Microsomal Triglyceride Transfer Protein Expression in Hepatocytes
AU Biessen, Erik A. L.; Sliedregt-Bol, Karen; Hoen, Peter A. Chr. T.; Prince, Perry; Van der Bilt, Erica; Valentijn, A. Rob P. M.; Meeuwenoord, Nico J.; Princen, Hans; Bijsterbosch, Martin K.; Van der Marel, Gijs A.; Van Boom, Jacques H.; Van Berkel, Theo J. C.
CS Division of Biopharmaceutics, Leiden/Amsterdam Center for Drug Research, Leiden University, Leiden, 2300 RA, Neth.
SO Bioconjugate Chemistry (2002), 13(2), 295-302 CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
AB In this study, we present the design and synthesis of an ***antisense*** ***peptide*** ***nucleic*** ***acid*** (asPNA) prodrug, which displays an improved biodistribution profile and an equally improved capacity to reduce the levels of target mRNA. The prodrug, K(GalNAc)2-asPNA, comprised of a 14-mer sequence complementary to the human microsomal triglyceride transfer protein (huMTP) gene, conjugated to a high-affinity tag for the hepatic asialoglycoprotein receptor (K(GalNAc)2). The prodrug was avidly bound and rapidly internalized by HepG2s. After iv injection into mice, K(GalNAc)2-asPNA accumulated in the parenchymal liver cells to a much greater extent than nonconjugated ***PNA*** (46% .+-. 1% vs. 3.1% .+-. 0.5% of the injected dose, resp.). The prodrug was able to reduce MTP mRNA levels in HepG2 cells by 35-40% ($P < 0.02$) at 100 nM in an asialoglycoprotein receptor- and sequence-dependent fashion. In conclusion, hepatocyte-targeted ***PNA*** prodrugs combine a greatly improved tropism with an enhanced local intracellular availability and activity, making them attractive therapeutics to lower the expression level of hepatic target genes such as MTP.
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 99 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:151028 CAPLUS
DN 136:384153
TI Overexpression of Protein-Tyrosine Phosphatase PTP.sigma. Is Linked to Impaired Glucose-Induced Insulin Secretion in Hereditary Diabetic Goto-Kakizaki Rats
AU Oestenson, Claes-Goeran; Sandberg-Nordqvist, Ann-Christine; Chen, Jie; Haellbrink, Mattias; Rotin, Daniela; Langel, Uelo; Efendic, Suad
CS Department of Molecular Medicine, Endocrine and Diabetes Unit, Karolinska Hospital and Institute, Stockholm, S-171 76, Swed.
SO Biochemical and Biophysical Research Communications (2002), 291(4), 945-950 CODEN: BBRCA9; ISSN: 0006-291X
PB Academic Press
DT Journal
LA English
AB The impaired glucose-induced insulin release in type 2 diabetes mellitus may be accounted for by reduced B-cell ATP/ADP ratio or decreased phosphorylation of proteins regulating exocytosis of insulin. This, in turn, could be due to enhanced phosphatase activity. Using in situ hybridization techniques to assess the expression of 11 different phosphotyrosine phosphatases (PTPases), known to be present in the B-cells, overexpression by approx. 60% of PTP.sigma. (also known as LAR-PTP2 or PTP NE-3) was demonstrated in pancreatic islets and liver of spontaneously type 2 diabetic Goto-Kakizaki (GK) rats. In agreement with these findings Western blot of islet lysates, using a polyclonal PTP.sigma. antiserum, showed increased amts. of the protein in GK relative to control rat islets. Exposure of isolated islets for 20 h to 5 .mu.M ***antisense*** to PTP.sigma., composed of an ***antisense*** ***PNA*** sequence of 15 bases linked to the cell penetrating peptide transportan, increased glucose-induced insulin secretion from GK rat islets, but not from control islets. In parallel, the amts. of the phosphatase decreased. In conclusion, increased expression of PTP.sigma. may be of pathogenetic significance for the defective insulin secretion in GK rat islets. (c) 2002 Academic Press.
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 100 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:142874 CAPLUS
DN 136:195329
TI Nucleic acid and corresponding protein sequences of human PHOR1-A11 and PHOR1-F5D6 useful in treatment and detection of cancer
IN Hubert, Rene S.; Raitano, Arthur B.; Faris, Mary; Challita-Eid, Pia M.; Ge, Wangmao; Jakobovits, Aya
PA Agensys, Inc., USA

SO PCT Int. Appl., 250 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2002014501 A2 20020221 WO 2001-US25862 20010817
WO 2002014501 A3 20030130 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 2001086541 A5 20020225 AU 2001-86541 20010817
PRAI US 2000-226241P P 20000817 WO 2001-US25862 W 20010817
AB The present invention relates to novel genes, designated PHOR1-A11 and PHOR1-F5D6, that are over-expressed in prostate, ovarian, bladder, and kidney cancers. A degenerate oligo PCR strategy was utilized to identify these two family members of the G-protein coupled receptors. Northern blot anal. of PHOR1-A11 and PHOR1-F5D6 gene expression in normal tissues shows a restricted expression pattern in adult tissues. The nucleotide and amino acid sequences of PHOR1-A11 and PHOR1-F5D6 are provided. PHOR1-A11 has the highest homol. to a Marmota olfactory receptor with 83% identity and 92% similarity over the entire Marmota 237 amino acid sequence; PHOR1-F5D6 has 100% amino acid homol. to an olfactory receptor protein predicted from PAC clone RP5-988G15. PHOR1-A11 is localized to human chromosome 1q43, suggesting that it is a candidate gene for hereditary prostate cancer, whereas PHOR1-F5D6 is localized to 7q33-q35, a region frequently amplified or rearranged in cancer. The tissue-related profile of PHOR1-A11 and PHOR1-F5D6 in normal adult tissues, combined with the over-expression obsd. in prostate and other tumors, shows that PHOR1-A11 and PHOR1-F5D6 is aberrantly over-expressed in at least some cancers, and thus serves as a useful diagnostic and/or therapeutic target for cancers of tissues such as prostate. The PHOR1-A11 or PHOR1-F5D6 gene or fragment thereof, or its encoded protein or a fragment thereof, can be used to elicit an immune response.

L9 ANSWER 101 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:142749 CAPLUS
DN 136:195323
TI Nucleic acid and corresponding protein sequences of human 83P2H3 and CaTrF2E11 useful in treatment and detection of cancer
IN Raitano, Arthur B.; Challita-Eid, Pia M.; Faris, Mary; Saffran, Douglas C.; Afar, Daniel E. H.; Levin, Elana; Hubert, Rene S.; Ge, Wangmao; Jakobovits, Aya
PA Agensys, Inc., USA
SO PCT Int. Appl., 270 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2002014361 A2 20020221 WO 2001-US25782 20010817
WO 2002014361 A3 20030925 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 2001085018 A5 20020225 AU 2001-85018 20010817 US 2003134784 A1 20030717 US 2001-932165 20010817
PRAI US 2000-226329P P 20000817 WO 2001-US25782 W 20010817
AB The present invention relates to novel genes, designated 83P2H3 and CaTrF2E11, that are over-expressed in prostate, ovarian, bladder, kidney, and lung cancers. A degenerate oligo PCR strategy was utilized to identify these two family members of the calcium transporters. Northern blot anal. of 83P2H3 and CaTrF2E11 gene expression in normal tissues shows a restricted expression pattern in adult tissues. The nucleotide and amino acid sequences of 83P2H3 and CaTrF2E11 are provided. 83P2H3 is localized to human chromosome 7q34, whereas CaTrF2E11 is localized to 12q24.1. The tissue-related profile of 83P2H3 and CaTrF2E11 in normal adult tissues, combined with the over-expression obsd. in prostate and other tumors, shows that 83P2H3 and CaTrF2E11 is aberrantly over-expressed in at least some cancers, and thus serves as a useful diagnostic and/or therapeutic target for cancers of tissues such as prostate. The 83P2H3 or CaTrF2E11 gene or fragment thereof, or its encoded protein or a fragment thereof, can be used to elicit an immune response.

L9 ANSWER 102 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:107608 CAPLUS
DN 136:162293
TI Enhanced targeting of DNA sequences by recombinase protein coated single-stranded homologous DNA analog probes
IN Belotserkovkii, Boris; Reddy, Gurucharan; Zarling, David A.
PA Pangene Corp., USA
SO PCT Int. Appl., 63 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2002010457 A2 20020207 WO 2001-US24092 20010731
WO 2002010457 C1 20020704 WO 2002010457 A3 20030925 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2002061530 A1 20020523 US 2001-919345 20010730 EP 1364047 A2 20031126 EP 2001-956078 20010731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2000-222272P P 20000731 US 2001-919345 A 20010730 WO 2001-US24092 W 20010731
AB The present invention is directed to methods and compns. for using DNA analog probes in increasing the efficiency of DNA targeting by recombinase coated nucleoprotein filaments. The present invention teaches novel methods and compns. that combine the traditional advantages of RecA coated filaments in catalyzing homol. searches with the utility of ***PNA*** (peptide nucleic acids) to bind DNA with a very high affinity and its ability to locally open the target DNA thereby improving the kinetics of RecA-mediated strand exchange. The invention finds use in modifying DNA sequences in target DNA, both in vivo and in vitro. Furthermore, the invention finds use in activating

homologous recombination, increasing homologous recombination frequencies and mutagenesis in target DNA. The invention also finds use in the stimulation of DNA repair enzymes to excise DNA sequences. Addnl., the invention finds use in gene cloning, gene family cloning of target DNA sequences and in activating cloning of homologous linear genomic DNA.

L9 ANSWER 103 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:51623 CAPLUS
DN 136:113769
TI ***Antisense*** oligonucleotides or peptide nucleic acids targeted to mammalian .beta.1 adrenoceptor-specific mRNA and their use in treatment of cardiovascular diseases
IN Phillips, M. Ian; Zhang, Yuan
PA University of Florida, USA
SO PCT Int. Appl., 186 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2002004623 A2 20020117 WO 2001-US21759 20010711
WO 2002004623 A3 20021227 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG US 6489307 B1 20021203
US 2000-614034 20000711 EP 1301593 A2 20030416 EP 2001-955810 20010711 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2000-614034 A 20000711 US 1998-152717 A2 19980914 WO 1999-US21007 A2 19990914 WO 2001-US21759 W 20010711
AB Disclosed are ***antisense*** oligonucleotide, polynucleotide, and ***peptide*** ***nucleic*** ***acid*** compds. that specifically bind to mammalian mRNA encoding a .beta.1-adrenoceptor polypeptide and that are useful in the control and/or treatment of cardiac dysfunction, hypertension, hypertrophy, myocardial ischemia, and other cardiovascular diseases in an affected mammal, and preferably, in a human subject. The ***antisense*** compds. disclosed herein, and pharmaceutical formulations thereof, provide sustained control of .beta.1-adrenoceptor expression over prolonged periods, and achieve therapeutic effects from as little as a single dose. Administration of these ***antisense*** compns. to approved animal models resulted in a decrease in blood pressure, but no significant change in heart rate. Use of such ***antisense*** compns. in the redn. of .beta.1-adrenoceptor polypeptides in a host cell expressing .beta.1-adrenoceptor-specific mRNA, and in the operation of medicaments for treating human and animal diseases, and in particular, hypertension and other cardiac dysfunction is also disclosed.

L9 ANSWER 104 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:46836 CAPLUS
DN 137:79206
TI Novel ***antisense*** agents based on peptide nucleic acids (PNAs)
AU Verheijen, Jeroen C.; van der Marel, Gijs A.; van Boom, Jacques H.
CS Leiden Institute of Chemistry, Gorlaeus Laboratories, Leiden, 2300 RA, Neth.
SO Innovation and Perspectives in Solid Phase Synthesis & Combinatorial Libraries: Peptides, Proteins and Nucleic Acids--Small Molecule Organic Chemistry Diversity, Collected Papers, International Symposium, 6th, York, United Kingdom, Aug. 31-Sept. 4, 1999 (2001), Meeting Date 1999, 145-148. Editor(s): Epton, Roger. Publisher: Mayflower Scientific Ltd., Kingswinford, UK. CODEN: 69CEGV; ISBN: 0-9515735-3-5
DT Conference
LA English
AB A symposium report. The solid phase synthesis of two novel classes of ***PNA*** based ***antisense*** agents with the ability to destroy the target RNA strand is described. The ribonucleolytic activity could be bestowed on ***PNA*** by the covalent attachment of the 5'-phosphorylated-2',5'-linked oligoadenylate (2-5A) to yield a 2-5A- ***PNA*** hybrid.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 105 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:46833 CAPLUS
DN 137:174765
TI Transportan, its analogues and their applications
AU Soomets, Ursel; Kilk, Kalle; Land, Tiit; Langel, Ulo
CS Department of Neurochemistry and Neurotoxicology, Arrhenius Laboratories, Stockholm University, Stockholm, S-106 91, Swed.
SO Innovation and Perspectives in Solid Phase Synthesis & Combinatorial Libraries: Peptides, Proteins and Nucleic Acids--Small Molecule Organic Chemistry Diversity, Collected Papers, International Symposium, 6th, York, United Kingdom, Aug. 31-Sept. 4, 1999 (2001), Meeting Date 1999, 131-136. Editor(s): Epton, Roger. Publisher: Mayflower Scientific Ltd., Kingswinford, UK. CODEN: 69CEGV; ISBN: 0-9515735-3-5
DT Conference; General Review
LA English
AB The properties of a chimeric membrane translocating peptide, transportan, and its analogs as well as their application as carrier vectors to deliver ***PNA*** ***antisense*** mols. into cells are discussed. Transportan is a chimeric peptide composed of galanin (1-12) in the N-terminus and the wasp venom peptide, mastoparan, in the C-terminus connected via Lys residue. The biotinylated transportan penetrated efficiently into cells as estd. by indirect immunofluorescence. Cellular penetration of transportan has been demonstrated to be galanin receptor independent and non-endocytic, as cellular uptake was not prevented by incubation at low temp., by crosslinking of cell surface membranes, by hyperosmolar sucrose soln. or by inhibitors of endocytosis. All transportan analogs have stable positions when they are buried in the membrane, but orientations in relation to the membrane surface differ. The effect of deletion analogs of transportan on the 125I-galanin binding to the galanin receptors could be an apparent effect reflecting the displacement of receptor from the complex with trimeric G-proteins resulting in obsd. lower affinity of the receptor towards galanin. A membrane translocating peptide, transportan, and its shorter analogs can be used to efficiently deliver ***PNA*** oligomers targeting different positions of human GalR1 mRNA into Bowes cells. Thus, transporter peptide- ***PNA*** constructs are promising candidates for ***antisense*** therapeutics.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 106 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:17628 CAPLUS
DN 137:103196
TI ***Antisense*** properties of ***peptide*** ***nucleic*** ***acid*** (***PNA***)

AU Koppelhus, Uffe; Nielsen, Peter E.
CS The Panum Institute, University of Copenhagen, Copenhagen, Den.
SO Antisense Drug Technology (2001), 359-374. Editor(s): Crooke, Stanley T. Publisher: Marcel Dekker, Inc., New York, N. Y. CODEN: 69CEBQ; ISBN: 0-8247-0566-1
DT Conference; General Review
LA English
AB A review presents significantly improved methods for delivery of ***peptide*** ***nucleic*** ***acid*** (***PNA***) to eukaryotic cells. Several of these methods have already yielded exciting ***antisense*** responses. The prospects of assessing the ***antisense*** potential, and the development of new gene therapeutic drugs are discussed. ***PNA*** was conceived as a pseudopeptide mimic of a triplex-forming oligonucleotide.
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 107 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:9334 CAPLUS
DN 136:244811
TI Identification of an import signal for, and the nuclear localization of, human lactoferrin
AU Penco, Silvana; Scarfi, Sonia; Giovine, Marco; Damonte, Gianluca; Millo, Enrico; Villaggio, Barbara; Passalacqua, Mario; Pozzolini, Marina; Garre, Cecilia; Benatti, Umberto
CS Department of Oncology, Biology and Genetics, University of Genoa, Genoa, Italy
SO Biotechnology and Applied Biochemistry (2001), 34(3), 151-159 CODEN: BABIEC; ISSN: 0885-4513
PB Portland Press Ltd.
DT Journal
LA English
AB Many different unique functions have been attributed to lactoferrin (Lf), including DNA and RNA binding, and transport into the nucleus, where Lf binds to specific sequences and activates transcription. A pentapeptide, Gly-Arg-Arg-Arg-Arg, corresponding to a region of the N-terminal portion of human Lf rich in basic amino acids, was synthesized and its intracellular localization was investigated. Peptide internalization was assayed using the rhodaminated form of the same mol. This N-terminal peptide sequence is able to be internalized within less than 10 min at concn. as low as 1 .mu.M, and its intracellular localization is nuclear, mainly nucleolar. Similar behavior was obsd. using peptides composed of either all L or D amino acids, the last one being a retro-inverse peptide. The internalization process does not involve an endocytotic pathway, since no inhibition of the uptake was obsd. at 4.degree.C. The kinetics of peptide internalization was also evaluated. The internalization properties of such a short Lf pentapeptide have been assayed for its ability to transport peptide nucleic acids (PNAs) inside cells in order to improve their efficacy. The abundant transmembrane transport and nuclear localization of the proposed peptide, deriving from hLf and, for the first time, identified as a nuclear localization signal, could be used as an alternative strategy to tackle the unsolved problem of intracellular accumulation of ***antisense*** and antigene drugs and for the development of new pharmacol. tools.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 108 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:935811 CAPLUS
DN 136:70084
TI Preparation of positively-charged ***peptide*** ***nucleic*** ***acid*** analogs as delivery agents with therapeutic and diagnostic applications
IN Katzhendler, Jehoshua; Schlossman, Ada; Najajreh, Yousuf; Gibson, Dan
PA Yissum Research Development Company of the Hebrew University of Jerusalem, Israel
SO PCT Int. Appl., 48 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2001098522 A2 20011227 WO 2001-IL570 20010622 WO 2001098522 A3 20020808 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 2001067788 A5 20020102 AU 2001-67788 20010622 EP 1292606 A2 20030319 EP 2001-945577 20010622 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2000-213706P P 20000623 WO 2001-IL570 W 20010622
OS MARPAT 136:70084
AB The present invention relates to novel types of peptide nucleic acids (PNAs) I wherein, R1 is hydrogen or a protecting group suitable for protecting an amino group; R2 is hydrogen or a protecting group suitable for the protection of a carboxyl group; and Bn is a protected or unprotected, natural or non-natural nucleobase other than thymine with improved properties. In particular, it relates to pos. charged ***PNA*** units having an ethylene linker between the backbone and the nucleobase, to oligonucleotide analogs comprising these units, to oligomers comprising these units, and to the use of pos. charged PNAs as novel delivery agents with therapeutic and diagnostic applications including for ***antisense*** therapy (no data). Mol. modeling of pos.-charged modified ***PNA*** is reported. Thus, t-Bu-N-(2-phthalimidoaminoethyl)-N-(2-hydroxyethyl)glycinate was prepd. and incorporated into ***PNA*** .

L9 ANSWER 109 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:923814 CAPLUS
DN 136:54025
TI Preparation of peptide nucleoside derivatives as ***antisense*** molecules
IN Inoue, Yoshihisa; Wada, Takehiko
PA Japan Science and Technology Corporation, Japan
SO PCT Int. Appl., 77 pp. CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2001096355 A1 20011220 WO 2001-JP5011 20010613 W: JP, US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR EP 1295891 A1 20030326 EP 2001-938631 20010613 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR US 2003208050 A1 20031106 US 2002-311048 20021212
PRAI JP 2000-177428 A 20000613 WO 2001-JP5011 W 20010613
AB Peptide nucleoside derivs. (***peptide*** ***nucleic*** ***acid*** , ***PNA***) represented by the following general formula [I; wherein Xs are the same or different and represent pyrimidine, purine nucleic acid base or deriv.(s) thereof; Y and Y' are the same or different and represent at least one amino acid

or amino acid deriv. selected from the group consisting of serine, ornithine, aspartic acid, glutamic acid, lysine, arginine, cysteine, .delta.-hydroxylysine, N-aminoethylglycine, N-aminoethylserine, N-aminoethyllysine, N-aminoethylornithine, N-aminoethylaspartic acid, N-aminoethylglutamic acid, homoglutamic acid, .beta.-thiocarbonylaspartic acid, .gamma.-thiocarbonylglutamic acid and .delta.-thiocarbonylhomoglutamic acid; R1 represents hydrogen or hydroxy; A represents a single bond, carbonyl or thiocarbonyl; m is an integer of from 0 to 5; and n is an integer of from 1 to 100.] are prepd. These compds. exhibit base specific recognition of nucleic acid base sequences with high affinity than natural nucleic acids and are not hydrolyzed easily by enzymes in vivo and useful as ***antisense*** mols. for gene therapy of cancer or genetic diseases (no data). They can also irreversibly control the on-off switching of gene expression from anti to syn or syn to anti direction by the influence of pH, light, temp., or concn. or presence of alk. earth or transition metal or sugar. Thus, 0.454 g pentachlorophenyl trichloroacetate and 0.174 mL diisopropylethylamine were added to a soln. of 0.129 g poly(L-glutamine) in 20 mL DMF at 0.degree. with stirring, and after 1 h treated with 0.267 g 5'-amino-5'-deoxyuridine, and heated at 60.degree. for 10 h to give 0.314 g poly[N.gamma.-(5'-deoxy-5'-aminouracyl)-L-glutamine].
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 110 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:886528 CAPLUS
DN 136:32634
TI Integrin-binding peptides and their use in increasing the efficiency of transformation of animal cells in vector vaccines for cancer, respiratory and heart diseases
IN Hart, Stephen Lewis
PA ICH Productions Ltd., UK
SO PCT Int. Appl., 108 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2001092542 A2 20011206 WO 2001-GB2394 20010530
WO 2001092542 A3 20030530 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI GB 2000-13089 A 20000530 GB 2000-13090 A 20000530
US 2001-287410P P 20010501
AB A method of increasing the efficiency of transformation of animal cells by binding the transforming the DNA to integrins is described. Peptides contg. an integrin-binding motif and a polylysine sequence for binding nucleic acid are used to bring the DNA in close contact with the cell. The ***peptide*** - ***nucleic*** ***acid*** complex may be delivered in a liposome. The nucleic acid preferably is or relates to a gene that is the target for gene therapy, gene vaccination or ***antisense*** therapy. The integrin binding component comprises an integrin-binding element and a spacer element. The integrin binding element is an integrin binding peptide and contains a cyclic conserved RGD amino acid sequence. The spacer element is a peptide that is longer and/or more hydrophobic than the dipeptide spacers GG (glycine-glycine) and GA (glycine-alanine), contains an .epsilon.-amino hexanoic acid, is the the N terminus of the integrin-binding element and has enhanced transfection activity. The lipid component preferably has membrane destabilizing or fusogenic properties like DOPE, DOTMA, DOSPA or combinations thereof. An embodiment of the present invention provides a ratio of lipid component (DOPE or DOTMA): integrin-binding/polycationic nucleic acid-binding component: nucleic acid of 0.75:4:1 by wt. or 0.5:1.25:0.25 nmol. Furthermore, the present invention provides a ratio of lipid component (DOPE or DOSPA): integrin-binding/polycationic nucleic acid-binding component: nucleic acid of 12:4:1 by wt. Transfection of confluent cells or other slowly dividing or non-dividing cells that are in contact with each other with a nucleic acid using a non-viral receptor targeted vector may be improved by the concurrent use of an agent that disrupts cell-cell junctions, like the calcium chelator EGTA (at concns. of less than 1 mM) or an antibody like anti-cadherin. The present invention can be used in a vaccines for neuroblastoma, leukemias and other cancers as well as for diseases affecting smooth muscle and cardiac muscle tissues as well as for respiratory dieases. These vectors are also useful as a kit for improved transfection activity and they can deliver very large DNA mols. to cells.

L9 ANSWER 111 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:828629 CAPLUS
DN 136:319920
TI Nuclear ***antisense*** effects of neutral, anionic and cationic oligonucleotide analogs
AU Sazani, Peter; Kang, Shin-Hong; Maier, Martin A.; Wei, Changfu; Dillman, Jennifer; Summerton, James; Manoharan, Muthiah; Kole, Ryszard
CS Lineberger Comprehensive Cancer Center and Department of Pharmacology, University of North Carolina, Chapel Hill, NC, 27599, USA
SO Nucleic Acids Research (2001), 29(19), 3965-3974 CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB The ***antisense*** activity of oligomers with 2'-O-Me (2'-O-Me) phosphorothioate, 2'-O-methoxyethyl (2'-O-MOE) phosphorothioate, morpholino and ***peptide*** ***nucleic*** ***acid*** (***PNA***) backbones was investigated using a splicing assay in which the modified oligonucleotides blocked aberrant and restored correct splicing of modified enhanced green fluorescent protein (EGFP) precursor to mRNA (pre-mRNA), generating properly translated EGFP. In this approach, ***antisense*** activity of each oligomer was directly proportional to up-regulation of the EGFP reporter. This provided a pos., quant. readout for sequence-specific ***antisense*** effects of the oligomers in the nuclei of individual cells. Nuclear localization of fluorescent labeled oligomers confirmed validity of the functional assay. The results showed that the free uptake and the ***antisense*** efficacy of neutral morpholino derivs. and cationic ***PNA*** were much higher than that of neg. charged 2'-O-Me and 2'-O-MOE congeners. The effects of the ***PNA*** oligomers were obsd. to be dependent on the no. of L-lysine (Lys) residues at the C-terminus. The expts. suggest that the ***PNA*** contg. Lys was taken up by a mechanism similar to that of cell-penetrating homeodomain proteins and that the Lys tail enhanced intracellular accumulation of ***PNA*** oligomer without affecting its ability to reach and hybridize to the target sequence.
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 112 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:815867 CAPLUS

DN 136:128433
TI Targeting of cancer-related proteins with ***PNA*** oligomers
AU Pooga, Margus; Langel, Ulo
CS Estonian Biocentre, Tartu, EE-51010, Estonia
SO Current Cancer Drug Targets (2001), 1(3), 231-239 CODEN: CCDTB9; ISSN: 1568-0096
PB Bentham Science Publishers Ltd.
DT Journal; General Review
LA English
AB A review. Aberrant gene expression is characteristic to all cancer cells and pathophysiol. in general. Selective inhibition of constitutively elevated expression of oncogenes provides an opportunity to hinder the proliferation of malignant cells. Small synthetic mols. that specifically interfere with transcription and/or translation have great potential as anticancer drugs. Currently first-generation ***antisense*** oligonucleotides are widely used to inhibit the oncogene expression. The second generation of ***antisense*** agents have been studied mainly in vitro. One of these agents, ***peptide*** ***nucleic*** ***acid*** (***PNA***) is an oligonucleotide mimic with a noncharged achiral polyamide backbone to which the nucleobases are linked. ***PNA*** oligomers bind tightly to complementary DNA or RNA and are very stable in biol. fluids. ***PNA*** can inhibit transcription and translation of target genes by specifically hybridizing to DNA or mRNA. The in vitro expts. showing inhibition of target protein expression by ***PNA*** have been followed by the first successful applications of ***PNA*** as an ***antisense*** agent in cultured cells and also in vivo. Hopefully this will lead to a wider use of ***PNA*** in the studies of cancer biol. and therapy.
RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 113 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:814939 CAPLUS
DN 136:232515
TI Synthesis of chiral phosphono- ***peptide*** ***nucleic*** ***acid*** monomers
AU Wu, Yun; Xu, Jie-Cheng
CS Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, 200032, Peop. Rep. China
SO Huaxue Xuebao (2001), 59(10), 1660-1666 CODEN: HHHPA4; ISSN: 0567-7351
PB Kexue Chubanshe
DT Journal
LA Chinese
OS CASREACT 136:232515
AB Peptide nucleic acids are the potential candidate of ***antisense*** and antigene. Chiral monomer backbones were efficiently prepd. by reductive amination of N-Boc or N-Fmoc protected L-alaninal with aminomethylphosphate di-Et ester and subsequent acylation of free secondary amines with thymine-1-ylacetic acid. After chem. switch of N-Boc to N-Fmoc, protected chiral phosphono- ***PNA*** monomers were obtained.

L9 ANSWER 114 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:776037 CAPLUS
DN 136:79154
TI Peptide-nucleic acids (PNAs): a tool for the development of gene expression modifiers
AU Gambari, Roberto
CS Department of Biochemistry and Molecular Biology, Ferrara, 44100, Italy
SO Current Pharmaceutical Design (2001), 7(17), 1839-1862 CODEN: CPDEFP; ISSN: 1381-6128
PB Bentham Science Publishers
DT Journal; General Review
LA English
AB A review. Peptide nucleic acids (PNAs) represent nucleic acid analogs with unique biochem. properties and of great interest for the development of therapeutic agents. The firstly designed and tested PNAs are mols. in which the sugar-phosphate backbone of DNA was replaced with a pseudopeptide chain constituted by N-(2-aminoethyl) glycine monomers. Nucleobases can be linked to this backbone through a carboxymethyl moiety, which allows to maintain a two atom spacer between the backbone and the bases. Since the first reports on PNAs based on N-(2-aminoethyl) glycine backbone, other ***PNA*** analogs have been synthesized, with the main purpose of improve biol. activities as well as stability and efficient delivery to target cells. Of great interest are chiral PNAs, ***PNA*** analogs bearing phosphate groups (PHONA), ***PNA*** -DNA and ***PNA*** -peptide chimeras, ***PNA*** linked to non-peptide vectors. PNAs hybridize to DNA and RNA with high efficiency following the Watson-Crick hybridization rules, forming highly stable ***PNA*** /DNA and ***PNA*** /RNA duplexes. In addn., homo-pyrimidine PNAs, as well as PNAs contg. a high pyrimidine:purine ratio, are able to bind to DNA or RNA forming highly stable (***PNA***)2-DNA triple helixes. Accordingly, therapeutic ***PNA*** and ***PNA*** analogs could act as antigene as well as ***antisense*** mols. In addn., recent studies provide evidences for the possible use of ***PNA*** -based therapeutic mols. as artificial promoters, as decoy or ribozyme facilitator. Among the therapeutic applications of ***PNA*** -based mols., the most promising include anti-cancer and anti-viral exptl. strategies, but activity of PNAs against bacteria and medically important parasitic organisms have been also reported.
RE.CNT 180 THERE ARE 180 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 115 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:765581 CAPLUS
DN 136:52555
TI CXCR3 expression on CD34+ hemopoietic progenitors induced by granulocyte-macrophage colony-stimulating factor: II. Signaling pathways involved
AU Tan, Jinquan; Liu, Anting; Jacobi, Henrik H.; Glue, Christian; Chen, Jing; Ryder, Lars P.; Madsen, Hans O.; Svejgaard, Arne; Skov, Per S.; Malling, Hans-Jorgen; Poulsen, Lars K.
CS Laboratory of Medical Allergology, Allergy Unit. and Laboratory for Tissue Typing, Department of Clinical Immunology, National University Hospital, Copenhagen, DK-2200, Den.
SO Journal of Immunology (2001), 167(8), 4405-4413 CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB CXCR3, known to have 4 ligands [IFN-.gamma. inducible protein 10 (.gamma.IP-10), monokine induced by IFN-.gamma. (Mig), I-TAC, and 6Ckine], is predominately expressed on memory/activated T lymphocytes. The authors recently reported that GM-CSF induces CXCR3 expression on CD34+ hemopoietic progenitors, in which .gamma.IP-10 and Mig induce chemotaxis and adhesion. Here they further report that stimulation with GM-CSF causes phosphorylation of Syk protein kinase, but neither Casitas B-lineage lymphoma (Cbl) nor Cbl-b in CD34+ hemopoietic progenitors can be blocked by anti-CD116 mAb. Specific Syk blocking generated by ***PNA*** ***antisense*** completely inhibits GM-CSF-induced CXCR3 expression in CD34+ progenitors at both mRNA and protein as well as at functional

levels (chemotaxis and adhesion). Cbl and Cbl-b blocking have no such effects. Thus, GM-CSF binds to its receptor CD116, and consequently activates Syk phosphorylation, which leads to induced CXCR3 expression. .gamma.IP-10 and Mig can induce Syk, Cbl, and Cbl-b phosphorylation in CD34+ progenitors by CXCR3. .gamma.IP-10 or Mig has induced neither chemotaxis nor adhesion in GM-CSF-stimulated Cbl-b-blocked CD34+ hemopoietic progenitors, whereas SDF-1.alpha. induces both chemotaxis and adhesion in these cells. Interestingly, .gamma.IP-10 and Mig can induce chemotaxis and adhesion in GM-CSF-stimulated Syk- or Cbl-blocked CD34+ hemopoietic progenitors. Thus, Cbl-b, but not Syk and Cbl phosphorylation, is essential for .gamma.IP-10- and Mig-induced chemotaxis and adhesion in CD34+ hemopoietic progenitors. This study provides a useful insight into novel signaling transduction pathways of the functions of CXCR3/.gamma.IP-10 and Mig, which may be esp. important in the cytokine/chemokine environment for mobilization, homing, and recruitment during proliferation, differentiation, and maturation of hemopoietic progenitor cells.
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 116 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:762857 CAPLUS
DN 135:335139
TI Pharmaceutical composition of modified ***PNA*** molecules
IN Christensen, Jeppe Viggo; Kristensen, Edward
PA Pantheco A/S, Den.
SO PCT Int. Appl., 33 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2001076636 A2 20011018 WO 2001-DK238 20010406 WO 2001076636 A3 20020228 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1296718 A1 20030402 EP 2001-921241 20010406 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI DK 2000-587 A 20000406 DK 2000-5 A 20000406 WO 2001-DK238 W 20010406
OS MARPAT 135:335139
AB The present invention concerns a ***peptide*** ***nucleic*** ***acid*** pharmaceutical compn. for use in combating infections.

L9 ANSWER 117 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:756007 CAPLUS
DN 136:200457
TI Synthesis of covalent oligonucleotide-peptide conjugates: the use of N-hydroxybenzotriazole esters
AU Kuznetsova, S. A.; Sumbatyan, N. V.; Malvy, C.; Bertrand, J.-R.; Harel-Bellan, A.; Korshunova, G. A.; Svinarchuk, F. P.
CS Kafedra Khim. Prirodnykh Soedinenii, Mosk. Gos. Univ. im. M. V. Lomonosova, Moscow, Russia
SO Vestnik Moskovskogo Universiteta, Seriya 2: Khimiya (2001), 42(4), 281-286 CODEN: VMUKA5; ISSN: 0579-9384
PB Izdatel'stvo Moskovskogo Universiteta
DT Journal
LA Russian
AB The covalent oligodeoxyribonucleotide-peptide conjugates were synthesized by condensation of 3' or 5'-phospho-N-oxybenzotriazoles of oligonucleotides with peptides as potent inhibitors and activators of genes expression. Two types of oligonucleotide-peptide conjugates were prepd. The first type conjugates contained as oligonucleotide fragment the ***antisense*** oligonucleotide, 5'-GAACACGCCATGTCGp-3', which is complementary to the mRNA segment of cell membrane protein of Friend murine leukemia virus and as peptide fragments [Leu5]-enkephalin and its [D-Ala2, Ual5] analog, and also the nucleotides based on modified .delta.-Orn chain. The second type conjugates included peptides GGG(PADALDDFDLDML)n (n = 2 or 3), which are a dimer or a trimer of the active domain of the transcription factor VP16, connected to the 3' or 5' end of the oligonucleotide 5'-GGAGGAGGAGGAGGGGGAGG-3', which gives stable triplexes with sequence of transport segment of HIV-2 VPX gene.

L9 ANSWER 118 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:749715 CAPLUS
DN 136:16848
TI Effect of Secondary Structure on the Thermodynamics and Kinetics of ***PNA*** Hybridization to DNA Hairpins
AU Kushon, Stuart A.; Jordan, Jason P.; Seifert, Jennifer L.; Nielsen, Henrik; Nielsen, Peter E.; Armitage, Bruce A.
CS Department of Chemistry, Carnegie Mellon University, Pittsburgh, PA, 15213-3890, USA
SO Journal of the American Chemical Society (2001), 123(44), 10805-10813 CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB The binding of a series of ***PNA*** and DNA probes to a group of unusually stable DNA hairpins of the tetraloop motif has been obsd. using absorbance hypochromicity (ABS), CD (CD), and a colorimetric assay for ***PNA*** /DNA duplex detection. These results indicate that both stable ***PNA*** -DNA and DNA-DNA duplexes can be formed with these target hairpins, even when the melting temps. for the resulting duplexes are up to 50 .degree.C lower than that of the hairpin target. Both hairpin/single-stranded and hairpin/hairpin interactions are considered in the scope of these studies. Secondary structures in both target and probe mols. are shown to depress the melting temps. and free energies of the probe-target duplexes. Kinetic anal. of hybridization yields reaction rates that are up to 160-fold slower than hybridization between two unstructured strands. The thermodn. and kinetic obstacles to hybridization imposed by both target and probe secondary structure are significant concerns for the continued development of ***antisense*** agents and esp. diagnostic probes.
RE.CNT 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 119 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:693344 CAPLUS
DN 135:269058
TI ***Peptide*** ***nucleic*** ***acid*** oligonucleotide analogs, methods of synthesis, and methods of use
IN Efimov, Vladimir; Fernandez, Joseph; Archdeacon, Dorothy; Archdeacon, John; Chakhmakhcheau, Oksana; Buryakova, Alla; Choob, Mikhail; Hondorp, Kyle
PA Active Motif, USA
SO PCT Int. Appl., 195 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------

PI WO 2001068673 A1 20010920 WO 2001-US8111 20010313
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 2001047414 A5 20010924 AU 2001-47414 20010313
EP 1263773 A1 20021211 EP 2001-920352 20010313
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2003059789 A1 20030327 US 2002-72975 20020209
PRAI US 2000-189190P P 20000314
US 2000-250334P P 20001130
US 2001-805296 A2 20010313
WO 2001-US8111 W 20010313
OS MARPAT 135:269058
AB The present invention relates generally to oligonucleotide analogs that include novel protein nucleic acid mols. (PNAs), particularly monomers, dimers, oligomers thereof and methods of making and using these oligonucleotide analogs. The PNAs of the present invention are characterized as including a variety of classes of mols., such as, for example, hydroxyproline peptide nucleic acids (HypNA) and serine peptide nucleic acids (SerNA). The invention includes monomers, homodimers, heterodimers, homopolymers and heteropolymers of these and other oligonucleotide analogs. The present invention includes method of using these oligonucleotide analogs in the detection and sepg. of nucleic acid mols., including uses that include the utilization of oligonucleotide analogs on a solid support. The present invention also includes methods for purifying or sepg. nucleic acids by hybridization with the oligonucleotides of the present invention, such as mRNA mols. The present invention also includes the use of oligonucleotides of the present invention in ***antisense*** and homologous recombination constructs and methods. Thus, hydroxyproline- and serine-based ***PNA*** derivs. were prepd. and the thermal stability of duplexes of these derivs. with oligonucleotides was detd. The use of such ***PNA*** derivs. in hybridization and mRNA isolation was demonstrated.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 120 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:653716 CAPLUS
DN 136:31564
TI Altering behavioral responses and dopamine transporter protein with ***antisense*** peptide nucleic acids
AU Tyler-McMahon, B. M.; Stewart, J. A.; Jackson, J.; Bitner, M. D.; Fauq, A.; McCormick, D. J.; Richelson, E.
CS Neuropsychopharmacology, Mayo Clinic, Jacksonville, FL, 32224, USA
SO Biochemical Pharmacology (2001), 62(7), 929-932 CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier Science Inc.
DT Journal
LA English
AB The dopamine transporter (DAT) plays a role in locomotion and is an obligatory target for amphetamines. We designed and synthesized an ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***) to rat DAT to examine the effect of this ***antisense*** mol. on locomotion and on responsiveness to amphetamines. Rats were injected i.p. daily for 9 days with either saline, an ***antisense*** DAT ***PNA*** , a scrambled DAT ***PNA*** , or a mismatch DAT ***PNA*** . On days 7 and 9 after initial motility measurements were taken, the animals were challenged with 10 mg/kg of amphetamine and scored for motility. On day 7, there was no significant difference between the baseline levels of activity of any of the groups or their responses to amphetamine. On day 9, the ***antisense*** ***PNA*** -treated rats showed a statistically significant increase in their resting motility ($P < 0.01$). When these rats were challenged with amphetamine, motility of the saline-, scrambled ***PNA*** -, and mismatch ***PNA*** -treated animals showed increases of 31-, 36-, and 20-fold, resp., while the ***antisense*** ***PNA*** -treated animals showed increases of only 3.4-fold ($P < 0.01$). ELISA results revealed a 32% decrease in striatal DAT in ***antisense*** ***PNA*** -treated rats compared with the saline, scrambled ***PNA*** , and mismatch ***PNA*** controls ($P < 0.001$). These results extend our previous findings that brain proteins can be knocked down in a specific manner by ***antisense*** mols. administered extracranially. Addnl., these results suggest some novel approaches for the treatment of diseases dependent upon the function of the dopamine transporter.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 121 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:637280 CAPLUS
TI Modified nucleobase containing peptide nucleic acids (PNAs)
AU Rajeev, Kallanthottathil G.; Maier, Martin A.; Manoharan, Muthiah
CS Department of Medicinal Chemistry, Isis Pharmaceuticals, Carlsbad, CA, 92008, USA
SO Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001), CARB-015 Publisher: American Chemical Society, Washington, D. C. CODEN: 69BUZP
DT Conference; Meeting Abstract
LA English
AB ***PNA*** exhibits high binding affinity for RNA and DNA targets and favorable ***antisense*** and strand invasion properties. With a goal of improving their pharmacodynamic and pharmacokinetic properties even further, we have developed efficient syntheses of modified nucleobase contg. ***PNA*** monomers and incorporated them into oligomers.

L9 ANSWER 122 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:628994 CAPLUS
DN 135:354318
TI In vitro stability of .alpha.-helical peptide nucleic acids (.alpha.PNAs)
AU Garner, P.; Sherry, B.; Moilanen, S.; Huang, Y.
CS Department of Chemistry, Case Western Reserve University, Cleveland, OH, 44106-7078, USA
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(17), 2315-2317 CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB .alpha.-Helical peptide nucleic acids (.alpha.PNAs) are synthetic mols. that merge the .alpha.-helix secondary structure of peptides with the codified Watson-Crick base pairing capability of nucleic acids. It is now demonstrated that .alpha.PNAs made up of either L- or D-amino acids are resistant to degrdn. by the proteases present in human serum. The increased stability of .alpha.PNAs towards proteases may be attributable to the presence of unnatural nucleoamino acid residues [-NHCH(CH2OCH2B)CO-, where B = thymine or cytosine] since the replacement of these amino acids by serine yields a control peptide that does break down in human serum. The stability of

.alpha.PNAs towards proteases makes them attractive candidates for further development as ***antisense*** agents.
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 123 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:624613 CAPLUS
DN 135:206471
TI Differentially expressed nucleic acids encoding tumor-associated proteins, kits, and methods for identification, assessment, prevention, and therapy of human prostate cancer
IN Schlegel, Robert; Endege, Wilson; Monahan, John E.
PA Millennium Predictive Medicine, Inc., USA
SO PCT Int. Appl., 975 pp. CODEN: PIXXD2
DT Patent
LA English PATENT NO. KIND DATE APPLICATION NO. DATE ----------- ---- -------- --------------- --------
PI WO 2001053836 A2 20010726 WO 2001-US2318 20010124
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR
PRAI US 2000-PV178525 20000124 US 2000-PV183245 20000217 US 2000-PV190139 20000316 US 2000-PV208126 20000531 US 2000-PV219705 20000718 US 2000-PV255160 20001213
AB This invention relates to newly discovered correlations between expression of certain nucleic acid markers and the cancerous state of human prostate cells. The levels of expression of individual markers and combinations of markers described herein correlates with the presence of prostate cancer or a pre-malignant condition in a patient. Methods are provided for detecting the presence of prostate cancer in a sample, the absence of prostate cancer in a sample, the stage of a prostate cancer, the metastatic potential of a prostate cancer, the indolence or aggressiveness of the cancer, and other characteristics of prostate cancer that are relevant to prevention, diagnosis, characterization and therapy of prostate cancer in a patient. Thousands of differentially-expressed cDNA markers are identified in subtracted cDNA libraries and by transcript profiling. [This abstr. record is the second of four records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L9 ANSWER 124 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:590807 CAPLUS
DN 136:227414
TI ***PNA*** interference mapping demonstrates functional domains in the noncoding RNA Xist
AU Beletskii, Anton; Hong, Young-Kwon; Pehrson, John; Egholm, Michael; Strauss, William M.
CS Harvard Institute of Human Genetics, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, 02115, USA
SO Proceedings of the National Academy of Sciences of the United States of America (2001), 98(16), 9215-9220 CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB The noncoding RNA Xist has been shown to be essential for X-chromosome inactivation and to coat the inactive X-chromosome (Xi). Thus, an important question in understanding the formation of Xi is whether the binding reaction of Xist is necessary for X-chromosome inactivation. In this article, we demonstrate the failure of X-chromosome silencing if the assocn. of Xist with the X-chromosome is inhibited. The chromatin-binding region was functionally mapped and evaluated by using an approach for studying noncoding RNA function in living cells that we call ***peptide*** ***nucleic*** ***acid*** (***PNA***) interference mapping. In the reported expts., a single 19-bp ***antisense*** cell-permeating ***PNA*** targeted against a particular region of Xist RNA caused the disruption of the Xi. The assocn. of the Xi with macro-histone H2A is also disturbed by ***PNA*** interference mapping.
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 125 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:545846 CAPLUS
DN 135:135935
TI Genetic engineering of nucleic acid sequences encoding cell-regulatory proteins useful for diagnostics and for improving cell viability
IN Katinger, Hermann; Grillari, Johannes; Grabherr, Reingard
PA Polymun Scientific Immunbiologische Forschung G.m.b.H., Austria
SO PCT Int. Appl., 29 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ----------- ---- -------- --------------- --------
PI WO 2001053472 A2 20010726 WO 2001-EP675 20010122 WO 2001053472 A3 20020214 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1248839 A2 20021016 EP 2001-902348 20010122 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2000-177216P P 20000121 WO 2001-EP675 W 20010122
AB The present invention relates to cell-regulatory proteins and to nucleotide sequences encoding said proteins wherein the proteins have been found to be potential tumor and/or senescense markers useful for medical diagnostics and addnl. having therapeutical potential as well as antiapoptotic properties useful for improving cell viability in cell culture technol. The invention further relates to antibodies directed against the cell-regulatory proteins and to their use in medical diagnostics and therapy. The invention further relates to methods for the manuf. and application of the cell-regulatory proteins and of the corresponding nucleotide sequences.

L9 ANSWER 126 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:435821 CAPLUS
DN 135:206946
TI ***PNA*** oligomers as tools for specific modulation of gene expression
AU Pooga, Margus; Land, Tiit; Bartfai, Tamas; Langel, Ulo
CS Department of Neurochemistry and Neurotoxicology, Arrhenius Laboratories, Stockholm University, Stockholm, S-10691, Swed.
SO Biomolecular Engineering (2001), 17(6), 183-192 CODEN: BIENFV; ISSN: 1389-0344
PB Elsevier Science B.V.

DT Journal; General Review
LA English
AB A review with 67 refs. Small synthetic mols. that can specifically inhibit translation and/or transcription have shown great promise as potential ***antisense*** /antigene drugs. ***Peptide*** ***nucleic*** ***acid*** (***PNA***), an oligonucleotide mimic, has a non-charged achiral polyamide backbone to which the nucleobases are attached. ***PNA*** oligomers are extremely stable in biol. fluids and they specifically hybridize to DNA or RNA in a complementary manner, forming very strong heteroduplexes. Some of the mRNAs have yet undetd. and possibly long half-lives, successful down regulation of gene expression by ***antisense*** oligonucleotides (ON) requires that the ***antisense*** agent is long lived. ***PNA*** fulfils this requirement better than phosphodiester or phsphorothioate ONs. ***PNA*** can inhibit transcription and translation of resp. genes by tight binding to DNA or mRNA. First in vitro expts. to specifically down regulate protein expression by ***PNA*** have been followed by successful ***antisense*** and antigene application of ***PNA*** oligomers in vivo. This review discusses the principles of the in vitro and in vivo use of ***PNA*** oligonucleotides.
RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 127 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:431510 CAPLUS
DN 135:313485
TI Intraperitoneal injection of ***antisense*** peptide nucleic acids targeted to the mu receptor decreases response to morphine and receptor protein levels in rat brain
AU McMahon, B. M.; Stewart, J. A.; Jackson, J.; Fauq, A.; McCormick, D. J.; Richelson, E.
CS Neuropsychopharmacology, Mayo Clinic, Jacksonville, FL, 32224, USA
SO Brain Research (2001), 904(2), 345-349 CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier Science B.V.
DT Journal
LA English
AB To det. the effectiveness of peptide nucleic acids (PNAs) in vivo, we designed and synthesized PNAs ***antisense*** to the mu receptor, the mol. target of morphine for inducing antinociception. Responsiveness of rats to morphine and the levels of mu receptor expression after treatment was measured. We delivered i.p. injections of ***antisense*** PNAs targeted to the mu receptor (AS-MOR), mismatch PNAs (AS-MOR MM), ***antisense*** PNAs targeted to the neurotensin receptor subtype 1 (AS-NTR1), or saline and then challenged the rats with 5 mg/kg morphine (i.p.) or neurotensin directly into the periaqueductal gray region of the brain. To avoid tolerance, sep. groups of animals were tested at 24, 48, and 72 h post-***PNA*** treatment. Only animals treated with the AS-MOR showed a redn. in their antinociceptive response to morphine. The lack of effect of morphine on the AS-MOR rats was profound at 24 and 48 h, but animals tested at 72 h were similar to control groups. At 24 h the AS-MOR rats had a significant 55% decrease in the levels of mu receptor in their periaqueductal gray region, while AS-MOR MM rats showed no significant change. Lastly, the AS-MOR rats continued to show a normal antinociceptive response to neurotensin. This study, therefore, provides addnl. support for the use of PNAs to target proteins within brain by systemically administered PNAs.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 128 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:404570 CAPLUS
DN 135:251551
TI Peptide Nucleic Acids Are Potent Modulators of Endogenous Pre-mRNA Splicing of the Murine Interleukin-5 Receptor-.alpha. Chain
AU Karras, James G.; Maier, Martin A.; Lu, Tao; Watt, Andrew; Manoharan, Muthiah
CS Department of Molecular and Cellular Pharmacology and Department of Medicinal Chemistry, ISIS Pharmaceuticals Incorporated, Carlsbad, CA, 92008, USA
SO Biochemistry (2001), 40(26), 7853-7859 CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB ***Antisense*** oligonucleotides (ASOs) that bind target pre-mRNA with high affinity have been shown to alter splicing patterns and offer promise as therapeutics. Previous studies have shown that ASOs fully modified with 2'-O-methoxyethyl (2'-O-MOE) sugar residues redirect constitutive and alternative splicing of the murine interleukin-5 receptor-.alpha. (IL-5R.alpha.) chain pre-mRNA in cells, resulting in inhibition of the membrane-bound isoform and enhanced expression of the sol. isoform. Here, we show that ***antisense*** peptide nucleic acids (PNAs) alter splicing of the IL-5R pre-mRNA in a fashion similar to their 2'-O-MOE-modified counterparts of the same sequence. Moreover, using ***PNA*** as the splicing modulator, the length of the ***antisense*** oligomer could be shortened from 20 to 15 nucleobase units to obtain a comparable effect. Treatment of cells with ***antisense*** ***PNA*** resulted in dose-dependent, specific downregulation of IL-5R.alpha. membrane isoform mRNA expression and enhanced levels of the sol. IL-5R.alpha. isoform transcript, with an EC50 equiv to that obsd. in parallel with the corresponding 2'-O-MOE ASO. The pronounced activity of ***antisense*** PNAs in modulating IL-5R.alpha. mRNA splicing obsd. in our study identifies these compds. as a promising new class of lower mol. wt. splicing modulators.
RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 129 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:369269 CAPLUS
DN 136:14903
TI Application of ***PNA*** and LNA oligomers to chemotherapy
AU Elayadi, Anissa N.; Corey, David R.
CS Departments of Pharmacology and Biochemistry, University of Texas Southwestern Medical Center, Dallas, TX, 75390-9041, USA
SO Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2001), 2(4), 558-561 CODEN: COIDAZ
PB PharmaPress Ltd.
DT Journal; General Review
LA English
AB A review with refs. ***Peptide*** ***nucleic*** ***acid*** (***PNA***) and locked nucleic acid (LNA) oligomers bind to complementary sequences with extremely high affinity. This high-affinity binding supports the hypothesis that they have advantages for targeting cellular nucleic acids and provide a better route for the development of oligonucleotide-based antiproliferative drugs. This article reviews the properties of ***PNA*** and LNA oligomers and describes the challenges that confront their application to cancer therapy.
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 130 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:367614 CAPLUS
DN 136:64722

TI Design and evaluation of oligonucleotide analogues
AU Leumann, Christian J.
CS Department of Chemistry & Biochemistry, University of Bern, Bern, CH-3012, Switz.
SO Chimia (2001), 55(4), 295-301 CODEN: CHIMAD; ISSN: 0009-4293
PB Neue Schweizerische Chemische Gesellschaft
DT Journal; General Review
LA English
AB A review. This article contains a short account of the chem. and biophys. properties of the oligonucleotide analogs bicyclo-DNA, tricyclo-DNA, [3.2.1]-DNA, [3.2.1]amide-DNA and the ***PNA*** analog OPA, recently developed in our lab. Emphasis is given to various aspects of conformational restriction as a designer tool for enhancing the performance of oligonucleotide analogs and for exploring the supramol. chem. of DNA. A short summary of current problems in the field of DNA triple-helix chem. as well as contributions from our lab. in this area concludes this communication.
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 131 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:321161 CAPLUS
DN 135:207063
TI HIV Rev peptides conjugated with peptide nucleic acids and their efficient binding to RRE RNA
AU Kumagai, I.; Takahashi, T.; Hamasaki, K.; Ueno, A.; Mihara, H.
CS Graduate School of Bioscience and Biotechnology, Department of Bioengineering, Tokyo Institute of Technology, Nagatsuta, Yokohama, 226-8501, Japan
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(9), 1169-1172 CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB HIV Rev peptides conjugated with peptide nucleic acids (PNAs) were designed and synthesized to develop a designing approach for a novel RNA-binding mol. The binding affinities of ***PNA*** -peptides with the Rev responsive element (RRE) RNA were detd. by the competition assay using a rhodamine-labeled Rev. The peptide conjugated with an ***antisense*** ***PNA*** (TGCGC) bound RRE RNA more efficiently than the mol. without the ***PNA*** or the peptide sequence. HIV Rev peptides conjugated with peptide nucleic acids (PNAs) were designed and synthesized to develop a designing approach for a novel RNA-binding mol. The binding affinities of ***PNA*** -peptides with the Rev responsive element (RRE) RNA were detd. by the competition assay using a rhodamine-labeled Rev. The peptide conjugated with an ***antisense*** ***PNA*** (TGCGC) bound RRE RNA more efficiently than the mol. without the ***PNA*** or the peptide sequence.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 132 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:309020 CAPLUS
DN 135:31691
TI Expression of highly selective sodium channels in alveolar type II cells is determined by culture conditions
AU Jain, Lucky; Chen, Xi-Juan; Ramosevac, Semra; Brown, Lou Ann; Eaton, Douglas C.
CS Department of Pediatrics and Center for Cell and Molecular Signaling, Emory University School of Medicine, Atlanta, GA, 30322, USA
SO American Journal of Physiology (2001), 280(4, Pt. 1), L646-L658 CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
AB Alveolar fluid clearance in the developing and mature lungs is believed to be mediated by some form of epithelial Na channels (ENaC). However, single-channel studies using isolated alveolar type II (ATII) cells have failed to demonstrate consistently the presence of highly selective Na+ channels that would be expected from ENaC expression. We postulated that in vitro culture conditions might be responsible for alterations in the biophys. properties of Na+ conductances obsd. in cultured ATII cells. When ATII cells were grown on glass plates submerged in media that lacked steroids, the predominant channel was a 21-pS nonselective cation channel (NSC) with a Na+-to-K+ selectivity of 1; however, when grown on permeable supports in the presence of steroids and air interface, the predominant channel was a low-conductance (6.6 .+-. 3.4 pS, n = 94), highly Na+-selective channel (HSC) with a ***PNa*** /PK >80 that is inhibited by submicromolar concns. of amiloride (K0.5 = 37 nM) and is similar in biophys. properties to ENaC channels described in other epithelia. To establish the relationship of this HSC channel to the cloned ENaC, we employed ***antisense*** oligonucleotide methods to inhibit the individual subunit proteins of ENaC (.alpha., .beta., and .gamma.) and used patch-clamp techniques to det. the d. of this channel in apical membrane patches of ATII cells. Overnight treatment of cells with ***antisense*** oligonucleotides to any of the three subunits of ENaC resulted in a significant decrease in the d. of HSC channels in the apical membrane cell-attached patches. Taken together, these results show that when grown on permeable supports in the presence of steroids and air interface, the predominant channels expressed in ATII cells have single-channel characteristics resembling channels that are assocd. with the coexpression of the three cloned ENaC subunits .alpha.-, .beta.-, and .gamma.-ENaC.
RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 133 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:260536 CAPLUS
DN 135:89702
TI Bactericidal ***antisense*** effects of peptide-***peptide*** ***nucleic*** ***acid*** conjugates
AU Good, Liam; Awasthi, Satish Kumar; Dryselius, Rikard; Larsson, Ola; Nielsen, Peter E.
CS Centerfor Genomics Research, Karolinska Institute, Stockholm, Swed.
SO Nature Biotechnology (2001), 19(4), 360-364 CODEN: NABIF9; ISSN: 1087-0156
PB Nature America Inc.
DT Journal
LA English
AB ***Antisense*** peptide nucleic acids (PNAs) can specifically inhibit Escherichia coli gene expression and growth and hold promise as anti-infective agents and as tools for microbial functional genomics. Here we demonstrate that chem. modification improves the potency of std. PNAs. We show that 9- to 12-mer PNAs, esp. when attached to the cell wall/membrane-active peptide KFFKFFKFFK, provide improvements in ***antisense*** potency in E. coil amounting to 2 orders of magnitude while retaining target specificity. Peptide- ***PNA*** conjugates targeted to rRNA and to mRNA encoding the essential fatty acid biosynthesis protein Acp prevented cell growth. The anti-acpP ***PNA*** at 2 .mu.M, concn. cured HeLa cell cultures non-invasively infected with E. coli K12 without any apparent toxicity to the human cells. These results indicate that

peptides can be used to carry ***antisense*** ***PNA*** agents into bacteria. Such peptide- ***PNA*** conjugates open exciting possibilities for anti-infective drug development and provide new tools for microbial genetics.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 134 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:240109 CAPLUS
DN 134:275750
TI Alteration of cellular proliferation or apoptosis by ***antisense*** modulation of mRNA splicing, polyadenylation, or degradation
IN Bennett, C. Frank; Cooke, Stanley T.; Manoharan, Muthiah; Wyatt, Jacqueline R.; Baker, Brenda F.; Monia, Brett P.; Freier, Susan M.; McKay, Robert; Karras, James G.
PA Isis Pharmaceuticals, Inc., USA
SO U.S., 39 pp., Cont.-in-part of U.S. Ser. No. 167,921. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI US 6210892 B1 20010403 US 1999-277020 19990326 US 6172216 B1 20010109 US 1998-167921 19981007 US 6214986 B1 20010410 US 1999-323743 19990602 CA 2345354 AA 20000413 CA 1999-2345354 19990928 WO 2000020432 A1 20000413 WO 1999-US22448 19990928 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 9962710 A1 20000426 AU 1999-62710 19990928 AU 755515 B2 20021212 EP 1119579 A1 20010801 EP 1999-949943 19990928 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO US 2001007025 A1 20010705 US 2000-734846 20001212 US 2002049173 A1 20020425 US 2000-734847 20001212 US 2003191300 A1 20031009 US 2002-302262 20021121
PRAI US 1998-167921 A2 19981007 US 1999-277020 A2 19990326 US 1999-323743 A 19990602 WO 1999-US22448 W 19990928 US 2000-734846 A1 20001212
AB The present invention provides compns. and methods for controlling the behavior of a cell, tissue or organism through ***antisense*** modulation of mRNA processing, using ***antisense*** compds. which do not support cleavage of the mRNA target. ***Antisense*** oligonucleotides with 2'-methoxyethoxy (2'-MOE), 2'-dimethylaminooxyethoxy (2'-DMAOE), 2'-dimethylaminoethoxyethoxy, 2'-acetamide, morpholino or ***peptide*** ***nucleic*** ***acid*** modifications were synthesized with phosphodiester or phosphorothioate backbone linkages. The modifications of ***antisense*** oligonucleotides were either uniform or gapped. Effects of modified ***antisense*** oligonucleotides on mRNAs were detd. for interleukin 5 (IL-5) receptor .alpha. and Bcl-x. Uniformly 2'-MOE oligonucleotides targeted to certain exons or intron/exon boundaries of the sol./membrane IL-5 receptor .alpha. caused reduced expression of the membrane form and increased expression of the sol. form. Reduced cell surface expression of IL-5 receptor .alpha. protein, induction of apoptosis, and inhibition of cell proliferation in response to IL-5 by the 2'-MOE ***antisense*** oligonucleotides were also measured. The Bcl-xl (long) isoform of Bcl-x inhibits apoptosis while the Bcl-xs (short) isoform antagonizes Bcl-xl. Uniformly 2'-MOE, phosphorothioate oligonucleotides (e.g. ISIS 22783) targeted to a region upstream of the 5' splice site of bcl-xl were found to increase the ratio of bcl-xs to bcl-xl. After ***antisense*** treatment with the highly active ISIS 22783, increased apoptosis of cells in response to UV stress, cisplatinum-induced cell death and taxol-induced cell death were quantitated. An ISIS 22783 analog with 2'-DMAOE had a similar effect on the bcl-xs/bcl-xl mRNA ratio.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 135 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:197666 CAPLUS
TI ***Peptide*** ***nucleic*** ***acid*** : Toward antibacterial drugs
AU Nielsen, Peter E.
CS Pantheco A/S and Department of Medical Biochemistry and Genetics, University of Copenhagen, Copenhagen, DK 2200, Den.
SO Abstracts of Papers - American Chemical Society (2001), 221st, CARB-013 CODEN: ACSRAL; ISSN: 0065-7727
PB American Chemical Society
DT Journal; Meeting Abstract
LA English
AB The pseudopeptide DNA mimic ***PNA*** (***peptide*** ***nucleic*** ***acid***) has many of the properties desired of a gene targeting reagent. It binds strongly and with high sequence specificity to complementary RNA and to homopurine and AT-rich targets in double stranded DNA, and can thereby specifically and efficiently inhibit translation and transcription, resp. Furthermore, ***PNA*** has extremely high biostability and is easy to chem. synthesize and modify. We recently demonstrated ***PNA*** mediated ***antisense*** down regulation of specific genes in a "leaky" E. coli strain (AS19) and also showed that PNAs targeted to specific sites of the rRNA inhibit bacterial growth. While these results indicated a possibility for developing ***PNA*** based antibacterial agents, they also clearly showed that derivs. with greatly improved bacterial uptake would be needed. The seminar will focus on recent advances in the efforts towards this goal. In particular, results relating to ***antisense*** gene regulation in E. coli (K12) using ***PNA*** -peptide conjugates, as well as pharmacokinetic data on antibacterial PNAs and in vivo results from a peritonitis/sepsis mouse model will be presented.

L9 ANSWER 136 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:172969 CAPLUS
DN 135:29564
TI Inhibition of gene expression in Entamoeba histolytica with ***antisense*** ***peptide*** ***nucleic*** ***acid*** oligomers
AU Stock, Roberto P.; Olvera, Alejandro; Sanchez, Ricardo; Saralegui, Andres; Scarfi, Sonia; Sanchez-Lopez, Rosana; Ramos, Marco A.; Boffa, Lidia C.; Benatti, Umberto; Alagon, Alejandro
CS Instituo de Biotechnological/UNAM, Morelos, 62210, Mex.
SO Nature Biotechnology (2001), 19(3), 231-234 CODEN: NABIF9; ISSN: 1087-0156
PB Nature America Inc.
DT Journal
LA English
AB Peptide nucleic acids (PNAs) may be a potent tool for gene function studies in medically important parasitic organisms, esp. those that have not before been accessible to mol. genetic knockout approaches. One such organism is Entamoeba histolytica, the causative agent of amebiasis, which infects about 500 million people and is the cause of clin. disease in over 40 million each year, mainly in the tropical and subtropical world.

We used ***PNA*** ***antisense*** oligomers to inhibit expression of an episomally expressed gene (neomycin phosphorotransferase, NPT) and a chromosomal gene (EhErd2, a homolog of Erd2, a marker of the Golgi system in eukaryotic cells) in axenically cultured trophozoites of e. histolytica. Measurement of NPT enzyme activity and EhErd2 protein levels, as well as measurement of cellular proliferation, revealed specific decreases in expression of the targe genes, and concomitant inhibition of cell growth, in trophozoites treated with micromolar concns. of unmodified ***antisense*** ***PNA*** oligomers.
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 137 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:152703 CAPLUS
DN 134:204116
TI Alpha-helical ***peptide*** ***nucleic*** ***acid*** , their preparation and diagnostic and therapeutic uses
IN Garner, Philip P.
PA USA
SO PCT Int. Appl., 32 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2001014398 A1 20010301 WO 2000-US21845 20000811
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1999-150637P P 19990825
AB The present invention relates to peptide-based nucleic acid surrogates (PNAs) having a repeating structure of (AAB-aan)m and a particular secondary structure that can bind to particular single-stranded nucleic acid targets. Preferably the peptide-based nucleic acid surrogate has an alpha-helical secondary structure (.alpha. ***PNA***). Also, the present invention relates to the method of forming peptide-based nucleic acid surrogates having a particular secondary structure. The nucleic acid surrogates may be utilized for therapeutic (***antisense*** , antigene), diagnostic (genetic), and mol. switching (.alpha. ***PNA*** chips) applications.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 138 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:129905 CAPLUS
DN 134:158469
TI Methods of bacterial gene function determination using peptide nucleic acids
IN Nielsen, Peter E.; Good, Liam
PA Den.
SO U.S., 34 pp., Cont.-in-part of U. S. Ser. 932,140. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI US 6190866 B1 20010220 US 1998-49190 19980327 US 6300318 B1 20011009 US 1997-932140 19970916
PRAI US 1997-932140 A2 19970916
AB Methods of and compns. for killing or inhibiting the growth of a bacteria are disclosed. Methods of determing bacterial gene functions are also disclosed. The methods comprise the use of ***peptide*** ***nucleic*** ***acid*** that is targeted to mRNA and/or rRNA. In certain embodiments, methods include the use of one or more sep. antibiotics.
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 139 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:122968 CAPLUS
DN 134:290855
TI Synthesis, Analysis, Purification, and Intracellular Delivery of Peptide Nucleic Acids
AU Braasch, Dwaine A.; Corey, David R.
CS Department of Pharmacology and Department of Biochemistry, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, 75390-9041, USA
SO Methods (San Diego, CA, United States) (2001), 23(2), 97-107 CODEN: MTHDE9; ISSN: 1046-2023
PB Academic Press
DT Journal
LA English
AB Peptide nucleic acids (PNAs) are nonionic DNA mimics. Their novel chem. properties may facilitate the development of selective and potent ***antisense*** and antigene strategies for regulating intracellular processes. Described herein are procedures for the synthesis, purifn., handling, and characterization of PNAs. A simple protocol for the lipid-mediated introduction of PNAs into in vitro cultures of mammalian cells is provided. (c) 2001 Academic Press.
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 140 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:116310 CAPLUS
DN 134:232071
TI Intrathecal administration of ***PNA*** targeting galanin receptor reduces galanin-mediated inhibitory effect in the rat spinal cord
AU Rezaei, Khadijeh; Xu, Isabella Shi; Wu, Wei-Ping; Shi, Tie-Jun; Soomets, Ursel; Land, Tiit; Xu, Xiao-Jun; Wiesenfeld-Hallin, Zsuzsanna; Hokfelt, Tomas; Bartfai, Tamas; Langel, Ulo
CS Department of Neurochemistry and Neurotoxicology, Arrhenius Laboratories, Stockholm University, Stockholm, Swed.
SO NeuroReport (2001), 12(2), 317-320 CODEN: NERPEZ; ISSN: 0959-4965
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Peptide nucleic acids (***PNA***) are nucleic acid analogs contg. neutral amide backbone, forming stable and tight complexes with cDNA/RNA. However, it is unclear whether unmodified ***PNA*** can efficiently penetrate neuronal tissue to act as ***antisense*** reagent. Here intrathecal (i.t.) injection of an unmodified ***antisense*** ***PNA*** complementary to the rat galanin receptor type I (GAIRI) mRNA is able to block the inhibitory effect of i.t. administered galanin on spinal nociceptive transmission. Autoradiog. ligand binding studies using [125I]galanin show that the unmodified ***PNA*** is able to reduce the d. of galanin binding sites in the dorsal horn. Thus, unmodified ***PNA*** applied i.t. appears to function as an effective ***antisense*** reagent in rat spinal cord in vivo.
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 141 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:90286 CAPLUS
DN 134:260794
TI Peptide nucleic acids as antibacterial agents via the ***antisense*** principle
AU E Nielsen, Peter
CS Center for Biomolecular Recognition, Department for Biochemistry and Genetics, Laboratory B, The Panum Institute, Copenhagen, DK-2200 N, Den.
SO Expert Opinion on Investigational Drugs (2001), 10(2), 331-341 CODEN: EOIDER; ISSN: 1354-3784
PB Ashley Publications Ltd.
DT Journal; General Review
LA English
AB A review with 57 refs. ***Peptide*** ***nucleic*** ***acid*** (***PNA***) is a peptide-like DNA mimic that was introduced almost ten years ago. It was immediately predicted that ***PNA*** would have a bright future in gene therapeutic drug development, but progress in this direction has been rather modest thus far. This is predominantly due to inefficient uptake of ***PNA*** by most living cells. However, within the past couple of years a variety of methods have been devised to address this problem and the stage should now be set for more rapid progress. Several studies have demonstrated ***antisense*** effects ex vivo in cells in culture and two reports on direct injection of ***PNA*** into the brain of rats are also interesting. Only a few studies have addressed the possible exploitation of the ***antisense*** principle for development of antibacterial drugs. However, the first in vitro results using antiribosomal RNA PNAs and ***antisense*** PNAs targeted to the .beta.-lactamase gene on Escherichia coli cultures were quite promising. Most recently, these preliminary studies have been extended to demonstrate in vivo efficacy of antibacterial PNAs in an E. coli peritonitis/sepsis mouse model. Therefore, ***PNA*** drug development again is rapidly picking up pace.
RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 142 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:78271 CAPLUS
DN 134:152616
TI Anti-growth factor receptor avidin fusion proteins as universal vectors for drug delivery
IN Morrison, Sherie L.; Penichet, Manuel L.; Coloma, Josephina M.; Pardridge, William M.; Shin, Seugn-Uon; Ng, Patrick P.
PA Regents of the University of California, USA
SO PCT Int. Appl., 81 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- -------------- --------
PI WO 2001007084 A1 20010201 WO 2000-US19827 20000721
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1999-145552P P 19990723
AB A fusion protein for delivery of a wide variety of agents to a cell via antibody-receptor-mediated endocytosis comprises a first segment and a second segment: the first segment comprising a variable region of an antibody that recognizes an antigen on the surface of a cell that after binding to the variable region of the antibody undergoes antibody-receptor-mediated endocytosis, and, optionally, further comprises at least one domain of a const. region of an antibody; and the second segment comprising a protein domain selected from the group consisting of avidin, an avidin mutein, a chem. modified avidin deriv., streptavidin, a streptavidin mutein, and a chem. modified streptavidin deriv. Typically, the antigen is a protein. Typically, the protein antigen on the surface of the cell is a receptor such as a transferrin receptor or an insulin receptor. The invention also includes an antibody construct incorporating the fusion protein that is either a heavy chain or a light chain together with a complementary light chain or heavy chain to form an intact antibody mol. The invention further includes targeting methods and screening methods.
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 143 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:64768 CAPLUS
DN 134:296071
TI Synthesis and RNAse L binding and activation of a 2-5A-(5')-DNA-(3')- ***PNA*** chimera, a novel potential ***antisense*** molecule
AU Verheijen, Jeroen C.; Chen, Ling; Bayly, Suzanne F.; Torrence, Paul F.; Van der Marel, Gijsbert A.; Van Boom, J. H.
CS Gorlaeus Laboratories, Leiden Institute of Chemistry, Leiden, 2300 RA, Neth.
SO Nucleosides, Nucleotides & Nucleic Acids (2000), 19(10-12), 1821-1830 CODEN: NNNAFY; ISSN: 1525-7770
PB Marcel Dekker, Inc.
DT Journal
LA English
AB Fully automated solid-phase synthesis gave access to a hybrid in which 5'-phosphorylated-2'-5'-linked oligoadenylate is connected to the 5'-terminus of DNA which, in turn, is linked at the 3'-end to ***PNA*** 2-5A-(5')-DNA-(3')- ***PNA*** chimera. This novel ***antisense*** mol. retains full RNase L activation potency while suffering only a slight redn. in binding affinity.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 144 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:48033 CAPLUS
DN 134:290359
TI A short phosphodiester window is sufficient to direct RNase H-dependent RNA cleavage by ***antisense*** ***peptide*** ***nucleic*** ***acid***
AU Malchere, Charlotte; Verheijen, Jeroen; Van Der Laan, Sander; Bastide, Lionel; Van Boom, Jacques; Lebleu, Bernard; Robbins, Ian
CS Institut de Genetique Moleculaire, UMR 5535 and EP 2030, CNRS, Montpellier, F-34293, Fr.
SO Antisense & Nucleic Acid Drug Development (2000), 10(6), 463-468 CODEN: ANADF5; ISSN: 1087-2906
PB Mary Ann Liebert, Inc.
DT Journal
LA English
AB The potential pharmacol. benefits of using ***peptide*** ***nucleic*** ***acid*** (***PNA***) as an ***antisense*** agent are tempered by its incapacity to activate RNase H. The mixed backbone oligonucleotide (ON) (or gapmer) approach, in which a short internal window of RNAse H-competent residues is embedded within an RNase H-incompetent ON has not been applied previously to ***PNA*** because ***PNA*** and DNA hybridize to RNA with very different helical structures, creating structural perturbations at the two ***PNA*** -DNA junctions. It

is demonstrated here for the first time that a short internal phosphodiester window within a ***PNA*** is sufficient to evoke the RNase H-dependent cleavage of a targeted RNA and to abrogate translation elongation in a well-characterized in vitro assay.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 145 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:20532 CAPLUS
DN 134:248902
TI ***Antisense*** imaging of gene expression in the brain in vivo
AU Shi, Ningya; Boado, Ruben J.; Pardridge, William M.
CS Department of Medicine, University of California School of Medicine, Los Angeles, CA, 90095-1682, USA
SO Proceedings of the National Academy of Sciences of the United States of America (2000), 97(26), 14709-14714 CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB ***Antisense*** radiopharmaceuticals could be used to image gene expression in the brain in vivo, should these polar mols. be made transportable through the blood-brain barrier. The present studies describe an ***antisense*** imaging agent comprised of an iodinated ***peptide*** ***nucleic*** ***acid*** (***PNA***) conjugated to a monoclonal antibody to the rat transferrin receptor by using avidin-biotin technol. The ***PNA*** was a 16-mer ***antisense*** to the sequence around the methionine initiation codon of the luciferase mRNA. C6 rat glioma cells were permanently transfected with a luciferase expression plasmid, and C6 exptl. brain tumors were developed in adult rats. The expression of the luciferase transgene in the tumors in vivo was confirmed by measurement of luciferase enzyme activity in the tumor ext. The [125I] ***PNA*** conjugate was injected i.v. in anesthetized animals with brain tumors; the animals were killed 2 h later for frozen sectioning of brain and film autoradiog. No image of the luciferase gene expression was obtained after the administration of either the unconjugated antiluciferase ***PNA*** or a ***PNA*** conjugate that was ***antisense*** to the mRNA of a viral transcript. In contrast, tumors were imaged in all rats administered the [125I] ***PNA*** that was ***antisense*** to the luciferase sequence and was conjugated to the targeting antibody. In conclusion, these studies demonstrate gene expression in the brain in vivo can be imaged with ***antisense*** radiopharmaceuticals that are conjugated to a brain drug-targeting system.
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 146 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:18675 CAPLUS
DN 135:89255
TI Non-invasive imaging of human telomerase activity-targeting enzyme in BNCT
AU Tsujino, H.; Imahori, Y.; Mineura, K.; Ono, K.; Fujii, R.; Ueda, S.
CS Department of Neurosurgery, Kyoto Prefectural University of Medicine, Japan
SO KURRI-KR (2000), KURRI-KR-54, 327-328 CODEN: KURRBF; ISSN: 1342-0852
DT Report
LA English
AB In the present study, we achieved non-invasive imaging of gene expression of human telomerase (hTRT) in brain tumors by systemic administration of ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***) and phosphorothioate-deriv. (S-oligomer) labeled with 11C as a positron emitter. The difference in the rate of incorporation of ***antisense*** between the tumor and the surrounding normal brain tissue is large enough to apply this technique practically to non-invasive imaging of gene expression in humans using positron emission tomog. (PET). We also expected that this technique can be used in developing the peculiar boron carrier in the neutron capture therapy.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 147 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:15936 CAPLUS
DN 134:193678
TI Peptide conjugates of oligonucleotides as enhanced ***antisense*** agents
AU Stetsenko, D. A.; Arzumanov, A. A.; Korshun, V. A.; Gait, M. J.
CS Laboratory of Molecular Biology, Medical Research Council, Cambridge, CB2 2QH, UK
SO Molecular Biology (Translation of Molekulyarnaya Biologiya (Moscow)) (2000), 34(6), 852-859 CODEN: MOLBBJ; ISSN: 0026-8933
PB MAIK Nauka/Interperiodica Publishing
DT Journal; General Review
LA English
AB A review with eighty-two refs. The use of synthetic oligonucleotides and their analogs to block gene expression by binding the complementary RNA sequences in cells, the ***antisense*** principle, has been limited by poor uptake of the agents by cells in culture. This review describes attempts to harness by chem. conjugation the ability of certain peptides that may cross membranes to enhance the cellular uptake of oligonucleotides. These include fusogenic and hydrophobic peptides, nuclear localization signals, receptor targeting and translocating peptides, and various combinations. We also outline briefly some popular methods of peptide-oligonucleotide conjugation. Finally, we review the use of noncovalent peptide additives and the recent studies of conjugates of ***peptide*** ***nucleic*** ***acid*** (***PNA***) with peptides.
RE.CNT 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 148 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:8700 CAPLUS
DN 134:204110
TI Computational procedures to explain the different biological activity of DNA/DNA, DNA/ ***PNA*** and ***PNA*** / ***PNA*** hybrid molecules mimicking NF-.kappa.B binding sites
AU Saviano, Michele; Romanelli, Alessandra; Bucci, Enrico; Pedone, Carlo; Mischiati, Carlo; Bianchi, Nicoletta; Feriotto, Giordana; Borgatti, Monica; Gambari, Roberto
CS Biocrystallography Research Centre, CNR and Centro Interuniversitario di Ricerca sui Peptidi Bioattivi, Naples, 80134, Italy
SO Journal of Biomolecular Structure & Dynamics (2000), 18(3), 353-362 CODEN: JBSDD6; ISSN: 0739-1102
PB Adenine Press
DT Journal
LA English
AB Peptide nucleic acids (***PNA***) have recently been proposed as alternative reagents in expts. aimed to the control of gene expression. In PNAs, the pseudopeptide backbone is composed of N-(2-aminoethyl)glycine units and therefore is

stable in human serum and cellular exts. PNAs hybridize with high affinity to complementary sequences of single-stranded RNA and DNA, forming Watson-Crick double helixes and giving rise to highly stable (***PNA***)2-RNA triplexes with RNA targets. Therefore, ***antisense*** and antigene PNAs have been synthesized and characterized. The major issue of the present paper is to describe some computational procedures useful to compare the behavior of ***PNA*** double stranded mols. and ***PNA*** /DNA hybrids with the behavior of regular DNA duplexes in generating complexes with DNA-binding proteins. The performed computational analyses clearly allow to predict that the lack of charged phosphate groups and the different shape of helix play a crit. role in the binding efficiency of NF-.kappa.B transcription factors. These computational analyses are in agreement with competitive gel shift and UV-cross linking expts. These expts. demonstrate that NF-.kappa.B ***PNA*** / ***PNA*** hybrids do not interact efficiently with proteins recognizing the NF-.kappa.B binding sites in genomic sequences. In addn., the data obtained indicate that the same NF-.kappa.B binding proteins recognize both the NF-.kappa.B DNA/ ***PNA*** and DNA/DNA hybrids, but the mol. complexes generated with NF-.kappa.B DNA/ ***PNA*** hybrids are less stable than those generated with NF-.kappa.B target DNA/DNA mols.
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 149 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:895604 CAPLUS
DN 134:187754
TI Ribozyme and ***peptide*** - ***nucleic*** ***acid*** - based gene therapy
AU Phylactou, L. A.
CS The Cyprus Institute of Neurology and Genetics, Nicosia, 1683, Cyprus
SO Advanced Drug Delivery Reviews (2000), 44(2-3), 97-108 CODEN: ADDREP; ISSN: 0169-409X
PB Elsevier Science Ireland Ltd.
DT Journal; General Review
LA English
AB A review with 70 refs. The recent discovery that RNA can act as a catalyst, apart from carrying genetic information, has given a new dimension to the field of gene therapy and has come to act synergistically with ***antisense*** technol. Ribozymes can be used to down-regulate (by RNA cleavage) or repair (by RNA trans-splicing) unwanted gene expression involved in disease. Hammerhead ribozymes have been used extensively to down-regulate gene expression in many diseases such as viral infections and cancer. Group I intron ribozymes on the other hand, have only been tried to repair inherited mutations but hold great promise for the future. Peptide nucleic acids (PNAs) technol. is another new technol., which is currently been tried to block gene or RNA function. Gene therapy protocols need significant improvements in order to be used routinely in patients and hopefully, these new players should prove valuable to identifying new therapies for several untreated diseases.
RE.CNT 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 150 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:868956 CAPLUS
DN 135:176118
TI Inhibition of neomycin phosphorotransferase expression in Entamoeba histolytica with ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***) oligomers
AU Stock, Roberto P.; Olvera, Alejandro; Scarfi, Sonia; Sanchez, Ricardo; Ramos, Marco A.; Boffa, Lidia C.; Benatti, Umberto; Landt, Olfert; Alagon, Alejandro
CS Instituto de Biotecnologia, Universidad Nacional Autonoma de Mexico (UNAM), Morelos, 62210, Mex.
SO Archives of Medical Research (2000), 31(4, Suppl.), S271-S272 CODEN: AEDEER; ISSN: 0188-4409
PB Elsevier Science Inc.
DT Journal
LA English
AB ***PNA*** oligomers were used as ***antisense*** agents for down-regulation of the bacterial gene for neomycin phosphotransferase (NPT) in E. histolytica in culture. The ***antisense*** ***PNA*** inhibited NPT activity by 70%; the scrambled control ***PNA*** oligomer did not have a significant effect. This study suggests that ***PNA*** oligomers may provide a valuable tool for genetic studies in E. histolytica and may be feasible gene-therapeutic agents against amebiasis.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 151 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:866533 CAPLUS
DN 134:111186
TI Inhibition of Gene Expression Inside Cells by Peptide Nucleic Acids: Effect of mRNA Target Sequence, Mismatched Bases, and ***PNA*** Length
AU Doyle, Donald F.; Braasch, Dwaine A.; Simmons, Carla G.; Janowski, Bethany A.; Corey, David R.
CS Departments of Pharmacology and Biochemistry, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, 75390-9041, USA
SO Biochemistry (2001), 40(1), 53-64 CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB Genome sequencing has revealed thousands of novel genes, placing renewed emphasis on chem. approaches for controlling gene expression. ***Antisense*** oligomers designed directly from the information generated by sequencing are one option for achieving this control. Here we explore the rules governing the inhibition of gene expression by peptide nucleic acids (PNAs) inside cells. PNAs are a DNA/RNA mimic in which the phosphate deoxyribose backbone has been replaced by uncharged linkages. Binding to complementary sequences is not hindered by electrostatic repulsion and is characterized by high rates of assocn. and elevated affinities. Here we test the hypothesis that the favorable properties of PNAs offer advantages for recognition of mRNA and ***antisense*** inhibition of gene expression in vivo. We have targeted 27 PNAs to 18 different sites throughout the 5'-untranslated region (5'-UTR), start site, and coding regions of luciferase mRNA. PNAs were introduced into living cells in culture as ***PNA*** -DNA-lipid complexes, providing a convenient high throughput method for cellular delivery. We find that PNAs targeted to the terminus of the 5'-UTR are potent and sequence-specific ***antisense*** agents. PNAs fifteen to eighteen bases in length were optimal inhibitors. The introduction of one or two mismatches abolished inhibition, and complementary PNAs targeted to the sense strand were also inactive. In striking contrast to effective inhibition by PNAs directed to the terminal region, PNAs complementary to other sites within the 5'-UTR do not inhibit gene expression. We also observe no inhibition by PNAs complementary to the start site or rest of the coding region, nor do we detect inhibition by PNAs that are highly C/G rich and possess extremely high affinities for their target sequences. Our results suggest that PNAs can block

binding of the translation machinery but are less able to block the progress of the ribosome along mRNA. The high specificity of ***antisense*** inhibition by PNAs emphasizes both the promise and the challenges for PNAs as ***antisense*** agents and provides general guidelines for using PNAs to probe the mol. recognition of biol. targets inside cells.
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 152 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:771861 CAPLUS
DN 134:263337
TI ***Antisense*** ***PNA*** effects in Escherichia coli are limited by the outer-membrane LPS layer
AU Good, Liam; Sandberg, Rickard; Larsson, Ola; Nielsen, Peter E.; Wahlestedt, Claes
CS Center for Genomics Research, Karolinska Institute, Stockholm, 171 77, Swed.
SO Microbiology (Reading, United Kingdom) (2000), 146(10), 2665-2670 CODEN: MROBEO; ISSN: 1350-0872
PB Society for General Microbiology
DT Journal
LA English
AB ***Antisense*** peptide nucleic acids (PNAs) can inhibit Escherichia coli gene expression and cell growth through sequence-specific RNA binding, and this opens possibilities for novel anti-infective agents and tools for microbial functional genomics. However, the cellular effects of PNAs are limited relative to effects in cell exts., presumably because of cell barrier components such as the outer-membrane lipopolysaccharide (LPS) layer or drug efflux pumps, both of which function to exclude antibiotics and other foreign mols. To evaluate the importance of such cellular factors on ***PNA*** effects, the authors developed a pos. assay for ***antisense*** inhibition by targeting the lac operon repressor and compared ***PNA*** susceptibilities in mutant and wild-type E. coli by assessing lacZ induction. Strains with defective LPS (AS19 and D22) were more permeable to the antibiotic nitrocefin and more susceptible to ***PNA*** than the wild-type. Also, ***PNA*** potency was improved in wild-type cells grown in the presence of certain cell-wall-permeabilizing agents. In contrast, the activities of the Acr and Emr drug efflux pumps were not found to affect ***PNA*** susceptibility. The results show that the LPS layer is a major barrier against cell entry, but PNAs that can enter E. coli are likely to remain active inside cells.
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 153 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:711205 CAPLUS
DN 134:187723
TI ***Antisense*** gene therapy
AU Chen, Yundi; Zeng, Yitao
CS Shanghai Institute of Medical Genetics, Shanghai Children's Hospital, Shanghai, 200040, Peop. Rep. China
SO Shengwu Gongcheng Jinzhan (2000), 20(3), 23-26, 29 CODEN: SGJHA2; ISSN: 1003-3505
PB Zhongguo Kexueyuan Wenxian Qingbao Zhongxin
DT Journal; General Review
LA Chinese
AB A review with 21 refs. Besides of ***antisense*** nucleic acid and ribozyme, a new kind of ***antisense*** drug, named ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***), was recently developed. The classical strategy for ***antisense*** therapy is to abrogate abnormal gene expression. However, a new approach by balance the ratio of gene expression was found to be work with the progress of the study in this field. Here we briefly described the new ideas in the strategy of ***antisense*** gene therapy, the ***antisense*** drug design, the stability of ***antisense*** drugs, and the future prospects in this field.

L9 ANSWER 154 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:707297 CAPLUS
DN 133:291966
TI Nucleic acids including human open reading frames encoding ORFX polypeptides
IN Shimkets, Richard A.; Leach, Martin
PA Curagen Corporation, USA
SO PCT Int. Appl., 5509 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2000058473 A2 20001005 WO 2000-US8621 20000331
WO 2000058473 A3 20010125 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 2000037745 A5 20001016 AU 2000-37745 20000331
EP 1165784 A2 20020102 EP 2000-916677 20000331 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRAI US 1999-127607P P 19990331 US 1999-127636P P 19990402 US 1999-127728P P 19990405 US 2000-540763 A2 20000330 WO 2000-US8621 W 20000331
AB The present invention provides 3161 different human open reading frames ORFX, encoding isolated polypeptides, as well as polynucleotides encoding ORFX and antibodies that immunospecifically bind to ORFX or any deriv., variant, mutant, or fragment of the ORFX polypeptides, polynucleotides or antibodies. The invention addnl. provides methods in which the ORFX polypeptide, polynucleotide and antibody are used in detection and treatment of a broad range of pathol. states, as well as to other uses.

L9 ANSWER 155 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:705130 CAPLUS
DN 133:277147
TI ***Antisense*** oligonucleotides labeled with stable isotopes and a method for detecting the same in drug analysis
IN Kawai, Gota; Wada, Akira; Takaku, Hiroshi
PA Nippon Sanso Corp., Japan
SO Eur. Pat. Appl., 24 pp. CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI EP 1041145 A2 20001004 EP 2000-106939 20000331 EP 1041145 A3 20031217 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO JP 2000290291 A2 20001017 JP 1999-94323 19990331 US 2003073075 A1 20030417 US 2000-535786 20000328 US 2003104433 A1 20030605 US 2002-214503 20020807
PRAI JP 1999-94323 A 19990331 US 2000-535786 A3 20000328
AB ***Antisense*** oligonucleotide sequences which enable the measurement of the distribution and structure of ***antisense*** oligonucleotide drugs in the body, with lapse of time, and a method of detecting these sequences are provided.

The ***antisense*** chains have a natural or non-natural nucleotide or ***peptide*** ***nucleic*** ***acid*** as a structure unit in which carbon atoms and nitrogen atoms are substituted by 13C and 15N, resp., and the ***antisense*** chains can be detected by nuclear magnet resonance spectrometry (NMR) such as 15N-1H or 13C-1H heteronuclide multiple quantum coherence spectrometry.

L9 ANSWER 156 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:608918 CAPLUS
DN 133:189608
TI Mouse and human GANP, a novel nuclear phosphoprotein with kinase activity and up-regulated in centrocytes of the germinal center and associated with MCM3, a protein essential for DNA replication
IN Sakaguchi, Nobuo; Kuwahara, Kazuhiko
PA Sumitomo Electric Industries, Ltd., Japan
SO PCT Int. Appl., 91 pp. CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2000050611 A1 20000831 WO 1999-JP4634 19990827 W: CA, JP, US
PRAI JP 1999-47035 A 19990224
AB A novel protein GANP with kinase activity, cDNAs, ***antisense*** oligonucleotides, and antibodies, are disclosed. Antigen (Ag) immunization induces formation of the germinal center (GC), with large, rapidly proliferating centroblasts in the dark zone, and small, nondividing centrocytes in the light zone. The authors identified a novel nuclear protein, GANP, that is up-regulated in centrocytes. The authors found that GANP was up-regulated in GC B cells of Peyer's patches in normal mice and in spleens from Ag-immunized mice. GANP-pos. cells appeared in the light zone of the GC, with coexpression of the peanut agglutinin (***PNA***) (***PNA***)-pos. B220-pos. phenotype. The expression of GANP was strikingly correlated with GC formation because Bc16-deficient mice did not show the up-regulation of GANP. GANP-pos. cells were mostly surrounded by follicular dendritic cells. Stimulation with anti-.mu. and anti-CD40 induced up-regulation of ganp mRNA as well as GANP protein in B220-pos. B cells in vitro. GANP is a 210 kDa protein localized in both the cytoplasm and nuclei, with a homologous region to Map80 that is assocd. with MCM3, a protein essential for DNA replication. Remarkably, GANP is assocd. with MCM3 in B cells and MCM3 is also up-regulated in the GC area. These results suggest that the up-regulation of GANP might participate in the development of Ag-driven B cells in GCs through its interaction with MCM3.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 157 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:595058 CAPLUS
DN 133:305962
TI Leptin contributes to the protection of human leukemic cells from cisplatinum cytotoxicity
AU Efferth, Thomas; Fabry, Ursula; Osieka, Rainhardt
CS Hospital for Internal Medicine IV, RWTH Aachen, Aachen, 52057, Germany
SO Anticancer Research (2000), 20(4), 2541-2546 CODEN: ANTRD4; ISSN: 0250-7005
PB International Institute of Anticancer Research
DT Journal
LA English
AB Leptin (ob gene) and its cognate receptor (obr) are relevant for fat metab. Obr shares homol. with the IL-6 signal transducer gp130 and is expressed in hematopoietic cells. Since cytokines and growth factors regulate both hematopoiesis and response to chemotherapy, we tested the hypothesis of whether leptin protects leukemic cells from cytotoxicity of cisplatinum. ***Antisense*** phosphorothioate oligodeoxynucleotides (ODNs) and ***antisense*** peptide nucleic acids (PNAs) complementary to the obr gene were first tested for their growth inhibitory activity in obr expressing leukemic cells. Liposome-mediated transfection of ODNs (1-2 .mu.M) or PNAs (0.01-1 .mu.M) inhibited growth up to 50%. Combination treatments of cisplatinum and 0.01 .mu.M ***PNA*** reduced growth more than cisplatinum alone. Vice versa, recombinant human leptin (rhL) diminished cisplatinum-induced growth inhibition. Finally, we investigated whether rhL affects cisplatinum-induced DNA damage and repair in the housekeeping gene .beta.-actin by means of real time TaqMan polymerase chain reaction. The rhL reduced DNA damage and increased DNA repair. The effects are, however, modest and leptin is probably not the only player in the armory of growth factors which affect drug resistance.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 158 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:475786 CAPLUS
DN 133:99558
TI Modified ***antisense*** oligonucleotides for inhibiting phosphodiesterase 4 gene expression and the therapeutic uses thereof
IN Dale, Roderic M. K.; Arrow, Amy; Thompson, Terry
PA Oligos Etc. Inc., USA
SO PCT Int. Appl., 48 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2000040714 A2 20000713 WO 1999-US29976 19991215
WO 2000040714 A3 20001102 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG CA 2357950 AA 20000713 CA 1999-2357950 19991215
EP 1141278 A2 20011010 EP 1999-968130 19991215 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO JP 2002534086 T2 20021015 JP 2000-592411 19991215 US 2003045490 A1 20030306 US 2002-76597 20020219
PRAI US 1998-223586 A 19981230 US 1999-364626 A 19990729
WO 1999-US29976 W 19991215
AB The invention provides end-blocked acid resistant ***antisense*** oligonucleotides targeted at inhibiting expression of genes coding for Phosphodiesterase 4 (PDE4). The oligonucleotides of this invention exhibit substantial stability at low pH, substantial resistance to nuclease degrdn., low toxicity and binding specificity both in vivo and in vitro. The invention further relates to the therapeutic uses of oligonucleotides of this invention in treatment of PDE4-mediated diseases.

L9 ANSWER 159 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:451993 CAPLUS
DN 133:290523
TI ***Antisense*** peptide nucleic acids
AU Nielsen, Peter E.

CS Center for Biomolecular Recognition Department for Biochemistry and Genetics Laboratory B, The Panum Institute, N Copenhagen, DK-2200, Den.
SO Current Opinion in Molecular Therapeutics (2000), 2(3), 282-287 CODEN: CUOTFO; ISSN: 1464-8431
PB PharmaPress Ltd.
DT Journal; General Review
LA English
AB A review with 36 refs. Within the past couple of years ***peptide*** ***nucleic*** ***acid*** (***PNA***) ***antisense*** and antigene technol. has entered the realm of biol. and preclin. studies. This is primarily due to the development of a no. of novel methods for more efficient delivery of ***PNA*** oligomers to eukaryotic cells. These methods have allowed ex vivo studies on cells in culture to be performed, and parallel in vivo studies are also slowly emerging. Although many issues still need to be resolved and several of the most recent results cannot be rationalized in a straight forward manner by existing knowledge, the immediate future should supply a more solid foundation for assessing the prospects of ***PNA*** ***antisense*** and antigene technol. both in the context of functional genomics and medicine.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 160 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:402744 CAPLUS
DN 133:208178
TI An experimental and theoretical study of the gas-phase decomposition of monoprotonated peptide nucleic acids
AU Flora, J. W.; Shillady, D. D.; Muddiman, D. C.
CS Department of Chemistry, Virginia Commonwealth University, Richmond, VA, USA
SO Journal of the American Society for Mass Spectrometry (2000), 11(7), 615-625 CODEN: JAMSEF; ISSN: 1044-0305
PB Elsevier Science Inc.
DT Journal
LA English
AB Peptide nucleic acids (PNAs) are DNA/RNA mimics which have recently generated considerable interest due to their potential use as ***antisense*** and antigene therapeutics and as diagnostic and mol. biol. tools. These synthetic biomols. were designed with improved properties over corresponding oligonucleotides such as greater binding affinity to complementary nucleic acids, enhanced cellular uptake, and greater stability in biol. systems. Because of the stability and unique structure of PNAs, traditional sequence confirmation methods are not effective. Alternatively, electrospray ionization coupled with Fourier transform ion cyclotron resonance mass spectrometry shows great potential as a tool for the characterization and structural elucidation of these oligonucleotide analogs. Extensive gas-phase fragmentation studies of a mixed nucleobase 4-mer (AACT) and a mixed nucleobase 4-mer with an acetylated N-terminus (N-acetylated AACT) have been performed. Gas-phase collision-induced dissocn. of PNAs resulted in water loss, cleavage of the methylene carbonyl linker contg. a nucleobase, cleavage of the peptide bond, and the loss of nucleobases. These studies show that the fragmentation behavior of PNAs resembles that of both peptides and oligonucleotides. Mol. mechanics (MM+), semiempirical (AM1), and ab initio (STO-3G) calcns. were used to investigate the site of protonation and det. potential low energy conformations. Computational methods were also employed to study prospective intramol. interactions and provide insight into potential fragmentation mechanisms.
RE.CNT 91 THERE ARE 91 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 161 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:398040 CAPLUS
DN 133:114502
TI ***Peptide*** ***nucleic*** ***acid*** (***PNA***): its medical and biotechnical applications and promise for the future
AU Ray, Arghya; Norden, Bengt
CS Department of Physical Chemistry, Chalmers University of Technology, Goeteborg, S 412 96, Swed.
SO FASEB Journal (2000), 14(9), 1041-1060 CODEN: FAJOEC; ISSN: 0892-6638
PB Federation of American Societies for Experimental Biology
DT Journal; General Review
LA English
AB A review with 120 refs. Synthetic mols. that can bind with high sequence specificity to a chosen target in a gene sequence are of major interest in medicinal and biotechnol. contexts. They show promise for the development of gene therapeutic agents, diagnostic devices for genetic anal., and as mol. tools for nucleic acid manipulations. ***Peptide*** ***nucleic*** ***acid*** (***PNA***) is a nucleic acid analog in which the sugar phosphate backbone of natural nucleic acid has been replaced by a synthetic peptide backbone usually formed from N-(2-amino-ethyl)-glycine units, resulting in an achiral and uncharged mimic. It is chem. stable and resistant to hydrolytic (enzymic) cleavage and thus not expected to be degraded inside a living cell. ***PNA*** is capable of sequence-specific recognition of DNA and RNA obeying the Watson-Crick hydrogen bonding scheme, and the hybrid complexes exhibit extraordinary thermal stability and unique ionic strength effects. It may also recognize duplex homopurine sequences of DNA to which it binds by strand invasion, forming a stable ***PNA*** -DNA- ***PNA*** triplex with a looped-out DNA strand. Since its discovery, ***PNA*** has attracted major attention at the interface of chem. and biol. because of its interesting chem., phys., and biol. properties and its potential to act as an active component for diagnostic as well as pharmaceutical applications. In vitro studies indicate that ***PNA*** could inhibit both transcription and translation of genes to which it has been targeted, which holds promise for its use for antigene and ***antisense*** therapy. However, as with other high mol. mass drugs, the delivery of ***PNA*** , involving passage through the cell membrane, appears to be a general problem.
RE.CNT 120 THERE ARE 120 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 162 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:382162 CAPLUS
DN 133:146440
TI Molecular Dynamics Simulations of ***PNA*** .cntdot.DNA and ***PNA*** .cntdot.RNA Duplexes in Aqueous Solution
AU Soliva, Robert; Sherer, Edward; Luque, F. Javier; Laughton, Charles A.; Orozco, Modesto
CS Departament de Bioquimica i Biologia Molecular Facultat de Quimica, Universitat de Barcelona, Barcelona, 08028, Spain
SO Journal of the American Chemical Society (2000), 122(25), 5997-6008 CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB Mol. dynamics simulations have been used to study the structure and flexibility of a DNA.cntdot. ***PNA*** duplex and a RNA.cntdot. ***PNA*** duplex in aq. soln. In this study, trajectories have been generated starting from three different conformations of the ***PNA*** .cntdot.DNA and ***PNA*** .cntdot.RNA duplexes: A-like, B-like, and PA/B-like. For the

DNA.cntdot. ***PNA*** duplex, the three trajectories converge within the nanosecond time scale to give structures resembling closely the PB model. The RNA.cntdot. ***PNA*** duplex trajectories started from A- and PA-forms converge to give structures resembling the PA model, but the trajectory begun from the B-like conformation leads to an unfolded duplex. Despite the similarity between PA and PB structures calcns. show the existence of important differences in terms of mol. recognition between both conformations. Anal. of the trajectories shows that the ***PNA*** backbone is very flexible provided that the backbone movements do not alter the positioning of the bases. It is found that ***PNA*** is able to distort the structure of RNA and esp. DNA strands during the formation of the ***PNA*** .cntdot.DNA and ***PNA*** .cntdot.RNA hybrids. The impact of these findings in antigene and ***antisense*** therapies is discussed.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 163 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:350041 CAPLUS
DN 133:276836
TI New ***PNA*** building blocks for ***antisense*** research
AU Jordan, Stephan; Schwemler, Christoph
CS Central Research, Bayer AG, Leverkusen, D-51368, Germany
SO Bioorganic Chemistry (1999), 262-271. Editor(s): Diederichsen, Ulf. Publisher: Wiley-VCH Verlag GmbH, Weinheim, Germany. CODEN: 68ZQAX
DT Conference; General Review
LA English
AB A review, with 8 refs. Synthesis of peptide nucleic acids (PNAs) as DNA analogs for ***antisense*** and mol. biol. purposes, properties of new homo-oligomers, synthesis and properties of hetero-oligomers, and future improvements are discussed.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 164 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:339531 CAPLUS
DN 133:217194
TI Peptide nucleic acids (***PNA***): toward gene therapeutic drugs
AU Nielsen, Peter E.
CS Center for Biomolecular Recognition, Department of Medical Biochemistry & Genetics, The Panum Institute, Copenhagen, 2200, Den.
SO Biomedical Chemistry (2000), 371-383. Editor(s): Torrence, Paul F. Publisher: John Wiley & Sons, Inc., New York, N. Y. CODEN: 69ABA6
DT Conference; General Review
LA English
AB A review with 43 refs. on the development of new ***antisense*** drugs for gene therapy of cancers.
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 165 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:335859 CAPLUS
DN 133:164314
TI Deoxynucleic Guanidine/ ***Peptide*** ***Nucleic*** ***Acid*** Chimeras: Synthesis, Binding and Invasion Studies with DNA
AU Barawkar, Dinesh A.; Kwok, Yan; Bruice, Thomas W.; Bruice, Thomas C.
CS Department of Chemistry and Biochemistry, University of California, Santa Barbara, CA, 93106, USA
SO Journal of the American Chemical Society (2000), 122(22), 5244-5250 CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB A fully automated solid-phase synthetic procedure for incorporation of pos. charged guanidinium linkages into otherwise neutral ***PNA*** sequences has been employed. These DNG/ ***PNA*** chimeras form [(DNG/ ***PNA***)2.cntdot.DNA] triplexes upon binding to single strand or duplex DNA (with accompanying D-loop for the latter). The [(DNG/ ***PNA***)2.cntdot.DNA] triplexes of DNG/ ***PNA*** T10, with DNA dA10, are more stable than DNA.cntdot.DNA triplexes [(T10)2.cntdot.dA10]. The binding of DNG/ ***PNA*** chimera with guanidinium linkages on both ends, with single strand length-matched complementary DNA under thermal melt conditions and with longer double strand DNA under isothermal conditions is sequence specific. The assocn. process of DNG/ ***PNA*** chimera with single strand DNA and strand invasion of longer ds-DNA is faster than the assocn. of ***PNA*** , with the same DNA targets, as evident by thermal hysteresis and gel retardation under isothermal conditions. The sequence specific and faster strand invasion of DNG/ ***PNA*** may extend the potential utility of ***PNA*** in diagnostics, biomol. probes, and ***antisense*** /antigene therapeutics.
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 166 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:327383 CAPLUS
TI Development of a high-throughput ***peptide*** ***nucleic*** ***acid*** synthesizer.
AU Roach, J. Shawn; Rayner, Simon; Mayfield, Lynn D.; Corey, David R.; Garner, Harold R.
CS Center for Biomedical Inventions - Dept. of Internal Medicine, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, 75235-8573, USA
SO Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000 (2000), BIOT-158 Publisher: American Chemical Society, Washington, D. C. CODEN: 69CLAC
DT Conference; Meeting Abstract
LA English
AB Peptide Nucleic Acids (PNAs) are synthetic analogs of DNA in which the phosphodiester backbone has been replaced with 2-aminoethyl glycine linkages, but maintaining the four natural nucleobases. A ***PNA*** strand will bind to DNA with the same sequence complementarity as std. DNA/DNA base paring, but ***PNA*** /DNA binding occurs more rapidly and more tightly than DNA/DNA binding. Much research has gone into the potential applications of PNAs as ***antisense*** and diagnostic agents. However, a major obstacle in ***PNA*** research becoming more widespread has been the high cost of the PNAs. A high throughput ***PNA*** synthesizer will afford an economy of scale and reduce the synthetic cost of PNAs. We report the development of a high throughput ***PNA*** synthesizer capable of producing up to 192 different PNAs in one synthesis run. The synthesizer is based on high throughput DNA synthesis technol. developed at the U. of Texas Southwestern Medical Center at Dallas to support the Human Genome Project. The synthesizer consists of an XY table, a series of valves plumbed to an injection head for reagent delivery, two vacuum chucks for reagent removal and a computer that controls the synthesis procedure. Synthesis is conducted in 96-well fritted filter plates, using std. solid phase Fmoc- ***PNA*** synthesis chem. The quality of the PNAs produced from the synthesizer is assessed using RP-HPLC and MALDI MS.

L9 ANSWER 167 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:303294 CAPLUS
DN 133:329462
TI ***Peptide*** ***nucleic*** ***acid*** delivery to human mitochondria. [Erratum to document cited in CA132:175761]
AU Chinnery, P. F.; Taylor, R. W.; Diekert, K.; Lill, R.; Turnbull, D. M.; Lightowlers, R. N.
CS Dep. Neurology, The Univ. Newcastle upon Tyne, NE2 4HH, UK
SO Gene Therapy (2000), 7(9), 813 CODEN: GETHEC; ISSN: 0969-7128
PB Nature Publishing Group
DT Journal
LA English
AB The incorrect extinction coeff. of 8900 M-1cm-1 was used for calcg. concns. of PNAs and their conjugates at 260 nm. Measurements should have been made using 97,900 M-1cm-1. Consequently, all concs. are effectively 11-fold more dil. than reported.

L9 ANSWER 168 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:298389 CAPLUS
DN 133:234000
TI Identification of a key target sequence to block human immunodeficiency virus type 1 replication within the gag-pol transframe domain
AU Sei, Shizuko; Yang, Quan-En; O'Neill, Dennis; Yoshimura, Kazuhisa; Nagashima, Kunio; Mitsuya, Hiroaki
CS HIV Clinical Interface Laboratory, SAIC-Frederick, NCI-Frederick Cancer Research and Development Center, Frederick, MD, 21702, USA
SO Journal of Virology (2000), 74(10), 4621-4633 CODEN: JOVIAM; ISSN: 0022-538X
PB American Society for Microbiology
DT Journal
LA English
AB Although the full sequence of the human immunodeficiency virus type 1 (HIV-1) genome has been known for more than a decade, effective genetic antivirals have yet to be developed. Here the authors show that, of 22 regions examd., one highly conserved sequence (ACTCTTTGGCAACGA) near the 3' end of the HIV-1 gag-pol transframe region, encoding viral protease residues 4 to 8 and a C-terminal Vpr-binding motif of p6Gag protein in two different reading frames, can be successfully targeted by an ***antisense*** ***peptide*** ***nucleic*** ***acid*** oligomer named PNAPR2. A disrupted translation of gag-pol mRNA induced at the PNAPR2-annealing site resulted in a decreased synthesis of Pr160Gag-Pol polyprotein, hence the viral protease, a predominant expression of Pr55Gag devoid of a fully functional p6Gag protein, and the excessive intracellular cleavage of Gag precursor proteins, hindering the processes of virion assembly. Treatment with PNAPR2 abolished virion prodn. by up to 99% in chronically HIV-1-infected H9 cells and in peripheral blood mononuclear cells infected with clin. HIV-1 isolates with the multidrug-resistant phenotype. This particular segment of the gag-pol transframe gene appears to offer a distinctive advantage over other regions in invading viral structural genes and restraining HIV-1 replication in infected cells and may potentially be exploited as a novel antiviral genetic target.
RE.CNT 156 THERE ARE 156 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 169 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:282744 CAPLUS
DN 133:155247
TI Dihydrotestosterone as a selective cellular/nuclear localization vector for anti-gene ***peptide*** ***nucleic*** ***acid*** in prostatic carcinoma cells
AU Boffa, Lidia C.; Scarfi, Sonia; Mariani, Maria Rita; Damonte, Gianluca; Allfrey, Vincent G.; Benatti, Umberto; Morris, Patricia L.
CS National Cancer Institute, IST, Genoa, 16132, Italy
SO Cancer Research (2000), 60(8), 2258-2262 CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Peptide nucleic acids (PNAs) are synthetic structural analogs of DNA and RNA that, if allowed to enter the cell, bind to the complementary polynucleotide sequence and inhibit DNA transcription and mRNA translation. Although PNAs have a very limited ability in penetrating nuclei of living cells, there are indications that covalent linkage of the ***PNA*** to appropriate vectors, e.g., a nuclear localization signal, permits access to the genome. Here we test the ability of dihydrotestosterone (T) covalently linked to ***PNA*** to act as a vector for targeting c-myc DNA to prostatic cancer cell nuclei. LNCaP cells, which express the androgen receptor gene, and DU145 cells, in which the androgen receptor gene is silent, offer a model to test this biol. active hormone as a cell-specific vector. T vector was covalently linked to the NH2-terminal position of a ***PNA*** complementary to a unique sequence of c-myc oncogene (PNAmyc-T). To localize PNAmyc-T and vector-free ***PNA*** within the cells, a rhodamine (R) group was attached at the COOH-terminal position (PNAmyc-R, PNAmyc-TR); cellular uptake was monitored by confocal fluorescence microscopy. PNAmyc-R was detected only in the cytoplasm of both prostatic cell lines, whereas PNAmyc-TR was localized in nuclei as well as in cytoplasm of LNCaP cells. In contrast, PNAmyc-TR uptake in DU145 cells was minimal and exclusively cytoplasmic. In LNCaP cells, MYC protein remained unchanged by exposure to vector-free PNAmyc, whereas a significant and persistent decrease was induced by PNAmyc-T. In DU145 cells, MYC expression was unaltered by PNAmyc with or without the T vector. Our data show that the T vector facilitates cell-selective nuclear localization of ***PNA*** and its consequent inhibition of c-myc expression. These findings suggest a strategy for targeting of cell-specific anti-gene therapy in prostatic carcinoma.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 170 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:234159 CAPLUS
DN 133:188549
TI ***Antisense*** technology for the specific modulation of gene expression
AU Bannwarth, Willi
CS Byk Gulden Pharmaceuticals, Konstanz, 78467, Germany
SO Collection Symposium Series (1999), 1(Future Aspects in Peptide Chemistry), 232-240 CODEN: CSYSFN
PB Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic
DT Journal
LA English
AB The ***antisense*** concept is an intriguing new strategy to specifically influence gene expressions. This article describes the basic principles of the technol. Furthermore, a new class of ***antisense*** mols. based on chimeric mols. composed of DNA and ***PNA*** entities is described. These oligomers have improved properties as compared to ***PNA*** mols. as such.
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 171 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:223282 CAPLUS
DN 133:145595
TI ***Antisense*** inhibition of .delta.-opioid receptor gene function in vivo by peptide nucleic acids
AU Fraser, Graeme L.; Holmgren, Janna; Clarke, Paul B. S.; Wahlestedt, Claes
CS AstraZeneca R and D, Montreal, QC, Can.
SO Molecular Pharmacology (2000), 57(4), 725-731 CODEN: MOPMA3; ISSN: 0026-895X
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Peptide nucleic acids (***PNA***) are synthetic analogs of DNA that hybridize to complementary oligonucleotide sequences with exceptional affinity and target specificity. The stability of ***PNA*** in biol. fluids together with the unique hybridization characteristics of these structures suggests that ***PNA*** may have considerable potential as ***antisense*** agents for exptl. use in vivo. To test this hypothesis, we attempted to modulate supraspinal .delta.-opioid receptor function in rats using ***PNA*** sequences designed to be complementary to a region of the rat .delta.-opioid receptor. Repeated i.c.v. administration of ***PNA*** over a period of 5 days significantly inhibited the antinociceptive response and locomotor response to selective .delta.-opioid receptor agonists. ***PNA*** attenuated .delta.-opioid receptor function in a sequence-specific, target-specific, and reversible manner characteristic of the functional inhibition caused by an ***antisense*** mechanism. There were no apparent toxicities arising from the ***PNA*** treatment based on the behavior of the animals and inspection of the treated tissues. Satn. binding studies on brain homogenates did not reveal any significant difference in receptor Bmax between treatment groups. However, [35S]guanosine-5'-O-(3-thio)triphosphate binding assays demonstrated a significant decrease in agonist efficacy in homogenates prepd. from ***antisense*** -treated rats. Taken together, these results demonstrate that peptide nucleic acids are effective ***antisense*** agents in vivo and suggest that ***PNA*** may be a useful alternative to phosphodiester or phosphorothioate oligonucleotides, or variants thereof, for detn. of gene function in vivo.
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 172 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:175918 CAPLUS
DN 132:232700
TI ***Peptide*** ***nucleic*** ***acid*** -oligoadenylate chimeras, their synthesis and use for inducing RNase L cleavage of RNA
IN Torrence, Paul F.; Van Boom, Jacques H.; Verheijen, Jeroen C.; Van Der Marel, Gijsbert A.
PA United States Dept. of Health and Human Services, USA; Leiden University
SO PCT Int. Appl., 41 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2000014219 A2 20000316 WO 1999-US20159 19990902
WO 2000014219 A3 20000706 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 9957034 A1 20000327 AU 1999-57034 19990902
PRAI US 1998-99173P P 19980904 WO 1999-US20159 W 19990902
AB Covalent conjugation of a 5'-phosphorylated-2',5'-linked oligoadenylate (2-5A) moiety to an ***antisense*** ***peptide*** ***nucleic*** ***acid*** oligomer (***PNA***) provides a novel chimeric reagent which effects the selective and specific cleavage of a selected target RNA. The 2-5A-***antisense*** ***PNA*** chimeras bind the target RNA with high specificity and affinity, and are stable to nucleases. The ***antisense*** portion of the chimera recruits a chosen RNA as substrate for cleavage, and the 2-5A portion of the chimera binds and activates RNase L, thus providing a new approach for the targeted ablation of a target mRNA and a redn. in expression of the protein which it specifies. The chimeric mols. are expected to have utility as research tools and as therapeutic agents. Thus, chimeric mols. comprising p5'A2'p5'A2'p5'A2'p5'A attached to ***PNA*** oligoadenylates were synthesized and shown to bind to poly(U) and stimulate its degrdn. by RNase L.

L9 ANSWER 173 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:139948 CAPLUS
DN 133:79208
TI Preparation of avidin-labeled gelatin nanoparticles as carriers for biotinylated ***peptide*** ***nucleic*** ***acid*** (***PNA***)
AU Coester, C.; Kreuter, J.; von Briesen, H.; Langer, K.
CS Biozentrum Niederursel, Institut fur Pharmazeutische Technologie, Johann Wolfgang Goethe-Universitat, Frankfurt am Main, 60439, Germany
SO International Journal of Pharmaceutics (2000), 196(2), 147-149 CODEN: IJPHDE; ISSN: 0378-5173
PB Elsevier Science B.V.
DT Journal
LA English
AB The possibility of prepg. uniform nanoparticles consisting of proteins such as gelatin followed by covalent linkage of avidin was investigated. Gelatin nanoparticles were prepd. by two step desolvation. Functional groups at the surface of the particulate system were quantified with site-specific reagents. The surface of the nanoparticles was thiolated and avidin was covalently attached to the nanoparticles via a bifunctional spacer at high levels. Biotinylated ***peptide*** ***nucleic*** ***acid*** (***PNA***) was effectively complexed by the avidin-conjugated nanoparticles. Avidin-conjugated protein nanoparticles should prove as potential carrier system for biotinylated drug derivs. in ***antisense*** therapy.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 174 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:138329 CAPLUS
DN 132:273649
TI Peptide nucleic acids: on the road to new gene therapeutic drugs
AU Nielsen, Peter E.
CS Center for Biomolecular Recognition, Department of Medical Biochemistry & Genetics, Biochemistry Laboratory B, Panum Institute, Copenhagen, DK-2200, Den.
SO Pharmacology & Toxicology (Copenhagen) (2000), 86(1), 3-7 CODEN: PHTOEH; ISSN: 0901-9928
PB Munksgaard International Publishers Ltd.
DT Journal; General Review

LA English
AB A review with .apprxeq. 40 refs. ***Peptide*** ***nucleic*** ***acid*** (***PNA***) is a DNA mimic based on a pseudopeptide (polyamide) backbone. ***PNA*** oligomers bind strongly and with high sequence specificity to complementary targets in RNA (or DNA), and they show very high biol. stability. Furthermore, studies in cell free systems have demonstrated potent ***antisense*** (inhibition of translation) and antigene (inhibition of transcription) activity of ***PNA*** . Recently, several studies reporting methods for cellular delivery of ***PNA*** as well as ***antisense*** effects of ***PNA*** in cells ex vivo and in rats have appeared. The potential of developing ***PNA*** derived gene therapeutic drugs is discussed.
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 175 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:124934 CAPLUS
DN 132:265428
TI New procedure of the Mitsunobu reaction as the key step in ***peptide*** ***nucleic*** ***acid*** (***PNA***) monomers synthesis
AU Falkiewicz, Bogdan; Kozyra, Agnieszka; Kolodziejczyk, Aleksandra S.; Liberek, Bogdan; Wisniewski, Kazimierz
CS Faculty of Chemistry, University of Gdansk, Gdansk, 80-952, Pol.
SO Nucleic Acids Symposium Series (1999), 42(Twentysixth Symposium on Nucleic Acids Chemistry, 1999), 9-10 CODEN: NACSD8; ISSN: 0261-3166
PB Oxford University Press
DT Journal
LA English
AB A symposium. PNAs are relatively novel DNA analogs, intensively studied due to their potential as gene-targeted drugs with antigene and ***antisense*** properties. In 1996 we elaborated a new method of synthesis of ***PNA*** monomer backbones based on the Mitsunobu reaction with N-tosyl-protected (Tos) amino acid esters as acidic components of the reaction. Since the method used for the Tos group removal requires conditions incompatible with various functional groups, here we modified the procedure by replacing the tosyl group with o-nitrobenzenesulfonyl (o-NBS) group. Using the new procedure we obtained protected ***PNA*** monomer backbones with various amino acid side chains. The pseudodipeptide secondary amine groups were then deprotected by thiolysis, and after std. work-up acylated with thymin-1-ylacetic acid, to give the protected monomers. Since the deprotection of the secondary amine group occurs under mild conditions, the procedure is of general applicability and allows various modifications of ***PNA*** structure by using diverse .beta.-amino alcs. and .alpha.-amino acid esters.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 176 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:70016 CAPLUS
DN 133:54261
TI Gene switching: analyzing a broad range of mutations using steric block ***antisense*** oligonucleotides
AU Morcos, Paul A.
CS Gene Tools, LLC, Corvallis, OR, 97333, USA
SO Methods in Enzymology (2000), 313(Antisense Technology, Part A), 174-189 CODEN: MENZAU; ISSN: 0076-6879
PB Academic Press
DT Journal
LA English
AB The gene switching method uses an ***antisense*** oligonucleotide to shut down the expression of an endogenous gene in tissue culture and replace it with plasmid-mediated expression of a desired gene construct. Luciferase reporter constructs showed that a 28-mer morpholino oligonucleotide had >2-fold activity than a ***peptide*** ***nucleic*** ***acid*** and .apprx.10-fold greater activity than the 2'-O-Me phosphorothioate directed against the same target. (c) 2000 Academic Press.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 177 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:70014 CAPLUS
DN 133:14
TI ***Antisense*** properties of ***peptide*** ***nucleic*** ***acid***
AU Nielsen, Peter E.
CS Department of Medical Biochemistry and Genetics, The Panum Institute, University of Copenhagen, Copenhagen, DK-2200, Den.
SO Methods in Enzymology (2000), 313(Antisense Technology, Part A), 156-164 CODEN: MENZAU; ISSN: 0076-6879
PB Academic Press
DT Journal; General Review
LA English
AB A review, with 46 refs. Cellular uptake, target selection, antigene, sequence considerations, design of ***peptide*** ***nucleic*** ***acid*** expts., and tech. hints are discussed. (c) 2000 Academic Press.
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 178 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:23192 CAPLUS
DN 132:74510
TI Oligonucleotide complementary to human ell factor-encoding gene for use as antiallergic agent
IN Yaguchi, Hiroshi; Kobata, Hideki
PA Ohtsuka Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 12 pp. CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ----
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PI JP 2000004881 A2 20000111 JP 1998-174599 19980622
PRAI JP 1998-174599 19980622
AB An oligonucleotide complementary to 3rd-7th codons of the stem cell factor (SCF)-encoding gene is provided for use as an antiallergic agent. The oligonucleotide can be modified by using phosphodiester linkages such as phosphorothioate linkages to improve the resistance to nuclease. The oligonucleotide may also be prepd. into peptide nucleic acids (PNS). The oligonucleotide was able to inhibit the biosynthesis of SCF in the cultured BALB/3T3 A31 cells.

L9 ANSWER 179 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:19325 CAPLUS
DN 132:78805
TI Preparation of new .delta.-amino acids possessing nucleic-acid base in the side chain and their derivatives
IN Shishido, Masahiko
PA Foundation for Scientific Technology Promotion, Japan
SO Jpn. Kokai Tokkyo Koho, 28 pp. CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ----
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PI JP 2000001478 A2 20000107 JP 1998-185584 19980615
PRAI JP 1998-185584 19980615
OS MARPAT 132:78805
AB The title compds. represented by formula R1NHCH(CH2CH2Bs)CH2OCH2COR2 (R1 = H, amino-protecting group; R2 = H, group derivatizing carboxy group; Bs = nucleic-acidic base such as Q, Q1, Q2, Q3, and Q4) or their salts are prepd. Also prepd. are (1) peptide nucleic acids (***PNA***) to which the above .delta.-amino acids are linked through an amide linkage and (2) these peptide nucleic acids hybridized with DNA or RNA. These peptide nucleic acids can bind to specific DNA or RNA sequences and are useful as ***antisense*** therapeutics for preventing the onset of diseases. Thus, N-benzoyladenine was condensed with tert-Bu 2-[(S)-4-tosyloxy-2- [(tert-butoxycarbonyl)amino]butoxy]acetate (prepn. from L-homoserine given) in the presence of K2CO3 and 18-crown-6-ether in DMF at room temp. for 7 h to give title compd. (I; R = Boc, R3 = tert-butyl) which was converted to the Fmoc-protected compd. (I; R = Fmoc, R3 = OH). The latter adenine deriv. was used to prep. a nonstandard ***peptide*** ***nucleic*** ***acid*** (II) by the solid phase method. When II was hybridized with T12 and T6CT5 (DNA), II-T12 and II-T6CT5 complexes exhibited melting temp. of 43 and 30.degree., resp.

L9 ANSWER 180 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:17192 CAPLUS
DN 132:175761
TI ***Peptide*** ***nucleic*** ***acid*** delivery to human mitochondria
AU Chinnery, P. F.; Taylor, R. W.; Diekert, K.; Lill, R.; Turnbull, D. M.; Lightowlers, R. N.
CS Department of Neurology, The University of Newcastle upon Tyne, NE2 4HH, UK
SO Gene Therapy (1999), 6(12), 1919-1928 CODEN: GETHEC; ISSN: 0969-7128
PB Stockton Press
DT Journal
LA English
AB Peptide nucleic acids (PNAs) are synthetic polynucleobase mols., which bind to DNA and RNA with high affinity and specificity. Although PNAs have enormous potential as ***anti*** - ***sense*** agents, the success of ***PNA*** -mediated gene therapy will require efficient cellular uptake and sub-cellular trafficking. At present these mechanisms are poorly understood. To address this, the authors have studied the uptake of biotinylated PNAs into cultured cell lines using fluorescence confocal microscopy. In human myoblasts, initial punctate staining was followed by the release of PNAs into the cytosol and subsequent localization and concn. in the nucleus. To det. whether PNAs could also be used as therapeutic agents for mtDNA disease, the authors attempted to localize PNAs to the mitochondrial matrix. When attached to the presequence peptide of the nuclear-encoded human cytochrome c oxidase (COX) subunit VIII, the biotinylated ***PNA*** was successfully imported into isolated organelles in vitro. Furthermore, delivery of the biotinylated peptide- ***PNA*** to mitochondria in intact cells was confirmed by confocal microscopy. These studies demonstrate that biotinylated PNAs can be directed across cell membranes and to a specific sub-cellular compartment within human cells - highlighting the importance of these novel mols. for human gene therapy.
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 181 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:813810 CAPLUS
DN 132:275552
TI ***Antisense*** ***PNA*** Tridecamers Targeted to the Coding Region of Ha-ras mRNA Arrest Polypeptide Chain Elongation
AU Dias, Nathalie; Dheur, Sonia; Nielsen, Peter E.; Gryaznov, Sergei; Van Aerschot, Arthur; Herdewijn, Piet; Helene, Claude; Saison-Behmoaras, Tula E.
CS Laboratoire de Biophysique, Museum National d'Histoire Naturelle, INSERM U201 CNRS UMR, 8646, Paris, 75231, Fr.
SO Journal of Molecular Biology (1999), 294(2), 403-416 CODEN: JMOBAK; ISSN: 0022-2836
PB Academic Press
DT Journal
LA English
AB We have previously described the rational design of mutation-selective ***antisense*** oligonucleotides targeted to codon 12 of oncogenic Ha-ras mRNA. In order to further improve the biol. efficacy of these unmodified oligonucleotides, we have studied three different classes of modifications: ***peptide*** ***nucleic*** ***acid*** backbone (***PNA***), sugar modification (2'-O-methyl) and phosphoramidate linkage (PN). We show that ***PNA*** is unique among the investigated steric blocking agents in its ability to specifically inhibit the translation of Ha-ras mRNA in vitro. The ***PNA*** -RNA hybrid (Tm=86.degree.), which is not dissocd. by cellular proteins and resists phenol extn. and urea denaturing conditions, specifically blocks the translation of mutated Ha-ras mRNA. A ***PNA*** tridecamer which forms with wild-type Ha-ras mRNA a duplex with a central mismatch had little effect on mRNA translation. Codon 12 is located close to the translation initiation site and hybridization of the ***PNA*** at this position may interfere with the assembly of the translation initiation complex. To test whether polypeptide chain elongation can also be blocked, we have targeted ***PNA*** tridecamers to codons in the 74, 128 and 149 regions. These PNAs form equally stable duplexes as that formed by the ***PNA*** targeted to the codon 12 region (ten G.cntdot.C base-pairs out of 13). We show that ***PNA*** -RNA duplexes block the progression of the 80 S ribosome. Therefore, it is possible to arrest translation with concomitant prodn. of a truncated protein by using duplex-forming ***PNA*** oligonucleotides targeted to a G+C-rich sequences. Our data demonstrate for the first time that a non-covalent duplex can arrest the translation machinery and polypeptide chain elongation. (c) 1999 Academic Press.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 182 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:795841 CAPLUS
DN 132:32476
TI Modified signal peptide sequence from Kaposi syndrome fibroblast growth factor, and uses thereof for the intracellular delivery of covalently linked ***antisense*** peptide nucleic acids
IN Nelson, John; Harriott, Patrick; Wallace, Andrew
PA The Queen's University of Belfast, UK
SO PCT Int. Appl., 33 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9964449 A2 19991216 WO 1999-GB1848 19990610 WO 9964449 A3 20021024 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM,

KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 9942819 A1 19991230 AU 1999-42819 19990610 EP 1086126 A1 20010328 EP 1999-955476 19990610 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI GB 1998-12376 A 19980610 GB 1998-14888 A 19980710
WO 1999-GB1848 W 19990610
AB The present invention relates to a new method of delivery of low mol. wt. mols. into a cell through the use of a modified signal peptide. Specifically, a modified analog of the signal peptide sequence from Kaposi syndrome fibroblast growth factor is used as a cell-permeant vehicle for the intracellular delivery of covalently linked ***antisense*** ***peptide*** ***nucleic*** ***acid*** sequences (PNAs). Modification of said peptide involves addn. of at least one pos. charged amino acid residue, such as lysine. The addn. of such pos. charged residues can serve as a linker group for the attachment of PNAs to the signal peptide thus increasing the no. of PNAs delivered by the signal peptide and therefore its functional efficiency. Extension of the signal peptide at the C or N terminus through the addn. of a single or multiple charged residue or analogs thereof will modify and improve signal peptide delivery function by increasing the soly. and cell permeability characteristics of the signal peptide.

L9 ANSWER 183 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:762229 CAPLUS
DN 132:190210
TI Detection of peptide nucleic acids in tissue extracts of treated animals by gel mobility shift assay
AU Jansen, K.; Richelson, E.
CS Laboratory of Neuropsychopharmacology, Mayo Foundation for Medical and Educational Research, Jacksonville, FL, USA
SO Journal of Biochemical and Biophysical Methods (2000), 42(1-2), 31-34 CODEN: JBBMDG; ISSN: 0165-022X
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB The authors have developed a sensitive and reproducible gel mobility shift assay to detect ***PNA*** oligomers in tissue of treated animals. ***PNA*** present in purified tissue exts. of treated animals is hybridized to a 33P-labeled DNA oligomer probe, and analyzed by polyacrylamide gel electrophoresis. The ***PNA*** -DNA hybrid migrates more slowly than the DNA probe alone and can be quantified relative to a std. curve. This detection method is useful for detecting PNAs in many different tissues, including brain, heart, kidney, liver, spleen, and serum, as well as cells in culture. This technique provides a very sensitive and reproducible method of detecting ***PNA*** oligomers in treated animals, and can be adapted to detect ***PNA*** oligomers in other samples, such as cells in culture.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 184 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:760681 CAPLUS
DN 132:160707
TI ***Antisense*** properties of ***peptide*** ***nucleic*** ***acid***
AU Larsen, H. J.; Bentin, T.; Nielsen, P. E.
CS Biochemistry Laboratory B, Department of Medical Biochemistry and Genetics, Center for Biomolecular Recognition, The Panum Institute, University of Copenhagen, Copenhagen, DK-2200, Den.
SO Biochimica et Biophysica Acta (1999), 1489(1), 159-166 CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier Science B.V.
DT Journal; General Review
LA English
AB A review with 48 refs. ***Peptide*** ***nucleic*** ***acid*** (***PNA***) is a nucleic acid mimic in which the deoxyribose phosphate backbone has been replaced by a pseudo-peptide polymer to which the nucleobases are linked. ***PNA*** -oligomers can be synthesized in relatively large amts., are highly stable in biol. environments, and bind complementary DNA and RNA targets with remarkably high affinity and specificity. Thus ***PNA*** possesses many of the properties desired for a good ***antisense*** agent. Until recently, limited uptake of ***PNA*** into cells has been the major obstacle for applying ***PNA*** as an ***antisense*** agent in cell cultures and in vivo. Here, the ***antisense*** properties of ***PNA*** in vitro and in vivo will be reviewed. In particular, we will focus on recent observations indicating that ***PNA*** equipped with or without various uptake moieties may function as an efficient and gene-specific inhibitor of translation in Escherichia coli and in certain mammalian cell types.
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 185 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:734739 CAPLUS
DN 132:88773
TI ***Peptide*** ***nucleic*** ***acid*** (***PNA***) ***antisense*** effects in Escherichia coli
AU Good, Liam; Nielsen, Peter E.
CS Karolinska Institute, Stockholm, S-17177, Swed.
SO Current Issues in Molecular Biology (1999), 1(2), 111-116 CODEN: CMBIF6; ISSN: 1467-3037
PB Caister Academic Press
DT Journal; General Review
LA English
AB A review with 25 refs. ***Antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***) can be used to control cell growth, gene expression and growth phenotypes in the bacteria Escherichia coli. PNAs targeted to the RNA components of the ribosome can inhibit translation and cell growth, and PNAs targeted to mRNA can limit gene expression with gene and sequence specificity. In an E. coli cell ext., efficient inhibition is obsd. when using ***PNA*** concns. in the nanomolar range, whereas micromolar concns. are required for inhibition in growing cells. A mutant strain of E. coli that is more permeable to antibiotics also is more susceptible to ***antisense*** PNAs than the wild type. This chapter details methods for testing the ***antisense*** activities of ***PNA*** in E. coli. As an example of the specific ***antisense*** inhibition possible, we show the effects of an anti-.beta.-galactosidase ***PNA*** in comparison to control PNAs. With improvements in cell uptake, ***antisense*** PNAs may find applications as antimicrobial agents and as tools for microbial functional genomics.
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 186 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:734737 CAPLUS
DN 132:89522
TI An introduction to ***peptide*** ***nucleic*** ***acid***
AU Nielsen, Peter E.; Egholm, Michael
CS The Panum Institute, Copenhagen, DK-2200, Den.
SO Current Issues in Molecular Biology (1999), 1(2), 89-104 CODEN: CMBIF6; ISSN: 1467-3037
PB Caister Academic Press
DT Journal; General Review
LA English

AB A review with 73 refs. ***Peptide*** ***Nucleic*** ***Acid*** (***PNA***) is a powerful new biomol. tool with a wide range of important applications. ***PNA*** mimics the behavior of DNA and binds complementary nucleic acid strands. The unique chem., phys. and biol. properties of ***PNA*** have been exploited to produce powerful biomol. tools, ***antisense*** and antigene agents, mol. probes and biosensors.
RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 187 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:710480 CAPLUS
DN 132:122866
TI Peptide nucleic acids: potential as ***antisense*** and antigene drugs
AU Eldrup, Anne B.; Nielsen, Peter E.
CS Department of Chemistry, University of Copenhagen, Copenhagen, Den.
SO Advances in Amino Acid Mimetics and Peptidomimetics (1999), 2, 221-245 CODEN: AAAMF9
PB JAI Press Inc.
DT Journal; General Review
LA English
AB A review with 84 refs. on properties, chem., and potential applications of ***peptide*** ***nucleic*** ***acid*** (***PNA***) is given. ***PNA*** is a DNA mimic with a pseudopeptide backbone. ***PNA*** oligomers bind strongly and with high specificity to sequence complementary RNA or DNA. Furthermore, homopyrimidine PNAs bind to complementary targets in double-stranded DNA by strand displacement. These properties of ***PNA*** combined with high biol. stability and ease of synthesis have made ***PNA*** highly interesting for the development of gene therapeutic drugs.
RE.CNT 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 188 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:700218 CAPLUS
DN 132:261107
TI Present and future of ***peptide*** ***nucleic*** ***acid***
AU Hu, Zhijun; Yang, Peiying
CS Institute of Microbiology and Epidemiology, Academy of Military Medical Sciences, Beijing, 100850, Peop. Rep. China
SO Junshi Yixue Kexueyuan Yuankan (1999), 23(3), 233-236 CODEN: JYKYEL; ISSN: 1000-5501
PB Junshi Yixue Kexueyuan Yuankan Bianjibu
DT Journal; General Review
LA Chinese
AB A review with 20 refs. ***Peptide*** ***nucleic*** ***acid*** (***PNA***) is a DNA mimic in which the nucleobases are attached to a pseudopeptide backbone. This achiral, uncharged and rather flexible peptide backbone permits stable hybridization to DNA and RNA and offers both ***antisense*** and antigene approaches to regulating gene expression. This review focuses on recent progress and future goals in developing ***PNA*** as a sequence-targeting drug. Topics include: synthesis of ***peptide*** ***nucleic*** ***acid*** (***PNA***), phys. properties of ***PNA*** , ***PNA*** hybridization with DNA, ***antisense*** effect, inhibition on the telomerase activity, effect on reverse transcriptase, activity in vivo, and prospects.

L9 ANSWER 189 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:673651 CAPLUS
DN 132:8740
TI An antibody-avidin fusion protein specific for the transferrin receptor serves as a delivery vehicle for effective brain targeting: initial applications in anti-HIV ***antisense*** drug delivery to the brain
AU Penichet, Manuel L.; Kang, Young-Sook; Pardridge, William M.; Morrison, Sherie L.; Shin, Seung-Uon
CS Department of Microbiology and Molecular Genetics and The Molecular Biology Institute, University of California, Los Angeles, CA, 90095, USA
SO Journal of Immunology (1999), 163(8), 4421-4426 CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB In the present study a novel Ab-avidin fusion protein has been constructed to deliver biotinylated compds. across the blood brain barrier. This fusion mol. consists of an Ab specific for the transferrin receptor genetically fused to avidin. The Ab-avidin fusion protein (anti-TfR IgG3-CH3-Av) expressed in murine myeloma cells was correctly assembled and secreted and showed both Ab- and avidin-related activities. In animal models, it showed much longer serum half-life than the chem. conjugate between OX-26 and avidin. Most importantly, this fusion protein demonstrated superior [3H]biotin uptake into brain parenchyma in comparison with the chem. conjugate. We also delivered a biotinylated 18-mer ***antisense*** ***peptide*** - ***nucleic*** ***acid*** specific for the rev gene of HIV-1 to the brain. Brain uptake of the HIV ***antisense*** drug was increased at least 15-fold when it was bound to the anti-TfR IgG3-CH3-Av, suggesting its potential use in neurol. AIDS. This novel Ab fusion protein should have general utility as a universal vehicle to effectively deliver biotinylated compds. across the blood-brain barrier for diagnosis and/or therapy of a broad range of CNS disorders such as infectious diseases, brain tumors as well as Parkinson's and Huntington's diseases.
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 190 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:669938 CAPLUS
DN 132:232647
TI In Vitro Transcriptional and Translational Block of the bcl-2 Gene Operated by ***Peptide*** ***Nucleic*** ***Acid***
AU Mologni, Luca; Nielsen, Peter E.; Gambacorti-Passerini, Carlo
CS Department of Experimental Oncology, Istituto Nazionale Tumori, Milan, 20133, Italy
SO Biochemical and Biophysical Research Communications (1999), 264(2), 537-543 CODEN: BBRCA9; ISSN: 0006-291X
PB Academic Press
DT Journal
LA English
AB The ***antisense*** and antigene activity of ***peptide*** ***nucleic*** ***acid*** (***PNA***) targeted to the human B-cell lymphoma (bcl)-2 gene was evaluated in vitro. Several PNAs complementary to different sequences of bcl-2, including the start codon and the 5'-untranslated region (5'-UTR), were tested. One ***PNA*** directed against the AUG start codon and another recognizing the 5'-UTR were able to specifically reduce Bcl-2 protein synthesis in a cell-free system; however, only partial inhibition (80 and 54%, resp.) was obtained when they were used singularly. Complete translation block was obtained with the simultaneous presence of both PNAs. A triplex-forming bis- ***PNA*** was targeted to a homopurine sequence on the coding strand of the bcl-2 cDNA. In an in vitro transcription assay this ***PNA*** specifically inhibited the transcription of bcl-2 at concns. as low as 300 nM, with the concomitant appearance of a truncated 200-base-long product.

These results demonstrate the ability of ***PNA*** to selectively modulate both translation and transcription of bcl-2 in vitro and suggest its potential use as an ***antisense*** and an antigene agent to down-regulate bcl-2 expression in tumors. (c) 1999 Academic Press.
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 191 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:612195 CAPLUS
DN 131:283408
TI A ***peptide*** ***nucleic*** ***acid*** -nuclear localization signal fusion that mediates nuclear transport of DNA
AU Branden, Lars J.; Mohamed, Abdalla J.; Smith, C. I. Edvard
CS Center for BioTechnology, Department of Biosciences, Karolinska Institutet, NOVUM, Huddinge, SE-14157, Swed.
SO Nature Biotechnology (1999), 17(8), 784-787 CODEN: NABIF9; ISSN: 1087-0156
PB Nature America
DT Journal
LA English
AB We have combined a ***peptide*** ***nucleic*** ***acid*** (***PNA***) with the SV40 core nuclear localization signal (NLS), to create a bifunctional ***PNA*** -NLS peptide. The ***PNA*** -NLS peptide increased the nuclear uptake of oligonucleotides and enhanced the transfection efficacy of plasmids. Gene expression from an enhanced green fluorescent protein plasmid and a lacZ plasmid was preserved when hybridized to ***PNA*** -NLS. In combination with the transfection agent polyethyleneimine, we have improved both the nuclear translocation of fluorescence-marked oligonucleotides, and the efficacy of plasmid transfection, up to eightfold. The technique obviates the use of cumbersome coupling procedures of the vector due to DNA- ***PNA*** duplex formation or displacement of the ***antisense*** plasmid DNA strand by a ***PNA*** mol.
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 192 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:539815 CAPLUS
TI Novel DNA and ***PNA*** analogs: Selectivity in DNA molecular recognition.
AU Ganesh, K. N.; Kumar, V. A.
CS Division of Organic Synthesis, National Chemical Laboratory, Pune-411008, India
SO Book of Abstracts, 218th ACS National Meeting, New Orleans, Aug. 22-26 (1999), CARB-081 Publisher: American Chemical Society, Washington, D. C. CODEN: 67ZJA5
DT Conference; Meeting Abstract
LA English
AB The advent of antigene/ ***antisense*** therapeutics has led to synthesis and study of innumerable chem. modifications of DNA structure in base and sugar-phosphate backbone.This presentation will focus on our recent work involving 5-amino-dU incorporated oligonucleotides and specificity in recognition of 5-amino-dU as a third base by A:T, T:A, G:C and C:G base pairs.We have also designed and synthesized conformationally restrained chiral ***PNA*** analogs based on 4-amino proline as a synthon.The selectivity in recognition of DNA by such chiral ***PNA*** analogs will be discussed.

L9 ANSWER 193 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:514962 CAPLUS
DN 131:333526
TI 2-5A- ***PNA*** complexes: a novel class of ***antisense*** compounds
AU Verheijen, J. C.; Bayly, S. F.; Player, M. R.; Torrence, P. F.; Van der Marel, G. A.; Van Boom, J. H.
CS Leiden Institute of Chemistry, Leiden, 2300 RA, Neth.
SO Nucleosides & Nucleotides (1999), 18(6 & 7), 1485-1486 CODEN: NUNUD5; ISSN: 0732-8311
PB Marcel Dekker, Inc.
DT Journal
LA English
AB This paper presents the fully automated solid phase synthesis of 2-5A- ***PNA*** hybrids. These stable ***antisense*** probes cause RNase L mediated hydrolysis of target RNA sequences.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 194 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:501547 CAPLUS
DN 132:61302
TI ***Antisense*** effects in Escherichia coli
AU Good, Liam; Nielsen, Peter E.
CS Karolinska Institutet, Stockholm, S-17177, Swed.
SO Peptide Nucleic Acids (1999), 213-220. Editor(s): Nielsen, Peter E.; Egholm, Michael. Publisher: Horizon Scientific Press, Norfolk, UK. CODEN: 67YLA6
DT Conference; General Review
LA English
AB A review with 19 refs. ***Antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***) can be used to control cell growth, gene expression and growth phenotypes in the bacterium Escherichia coli. PNAs targeted to the RNA components of the ribosome can inhibit translation and cell growth, and PNAs targeted to mRNA can limit gene expression with gene and sequence specificity. For in vitro expts., efficient inhibition is obsd. when using ***PNA*** concns. in the nanomolar range, and for in vivo expts. the concns. required are in the micromolar range. A mutant strain of E. coli that is more permeable to antibiotics is more susceptible to ***antisense*** PNAs than wildtype cells. This chapter details methods for testing the ***antisense*** activities of ***PNA*** in E. coli. As an example of specific ***antisense*** inhibition, we show the effects of an anti-.beta.-galactosidase ***PNA*** in comparison to control PNAs. With improvements in cell uptake, ***antisense*** PNAs may find applications as antimicrobial agents and as a tool for microbial functional genomics.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 195 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:501533 CAPLUS
DN 132:194633
TI ***PNA*** /DNA chimeras
AU Uhlmann, Eugen; Greiner, Beate; Breipohl, Gerhard
CS Hoechst Marion Roussel Deutschland GmbH Chemical Research G 838, Frankfurt am Main, D-65926, Germany
SO Peptide Nucleic Acids (1999), 51-70. Editor(s): Nielsen, Peter E.; Egholm, Michael. Publisher: Horizon Scientific Press, Norfolk, UK. CODEN: 67YLA6
DT Conference
LA English
AB A convenient method for the solid-support synthesis of ***PNA*** /DNA chimeras is described which makes use of monomethoxytrityl/acyl-protected monomeric building blocks. The acid-labile monomethoxytrityl (Mmt) group is employed for the temporary protection of the amino function of aminoethyl-glycine, while the exocyclic amino functions of the nucleobases are protected with ammonia-cleavable acyl protecting groups. This orthogonal protecting-group strategy is fully compatible with

the std. phosphoramidite DNA synthesis method. The resulting ***PNA*** /DNA chimeras obey the Watson-Crick rules on binding to complementary DNA and RNA. Binding affinity of the ***PNA*** -DNA chimeras strongly depends on the ***PNA*** :DNA ratio. The ***PNA*** /DNA chimeras bind with higher affinity to RNA than to DNA, and the type of linking moiety between ***PNA*** and DNA could be adjusted to obtain optimal binding affinity. In addn. to their promising binding properties, ***PNA*** -DNA chimeras can also assume biol. functions, such as a primer function for DNA polymerases. Pure PNAs cannot induce RNase H cleavage of target RNA, which often supports the biol. efficacy of ***antisense*** agents. In contrast, the DNA- ***PNA*** chimeras are able to stimulate cleavage of the target RNA by RNase H on formation of a RNA chimera duplex.
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 196 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:501530 CAPLUS
DN 131:307924
TI An introduction to ***PNA***
AU Nielsen, Peter E.; Egholm, Michael
CS The Panum Institute, Copenhagen N, DK-2200, Den.
SO Peptide Nucleic Acids (1999), 1-19. Editor(s): Nielsen, Peter E.; Egholm, Michael. Publisher: Horizon Scientific Press, Norfolk, UK. CODEN: 67YLA6
DT Conference; General Review
LA English
AB A review with 72 refs. on structure, properties, backbone and nucleobase modifications of Peptide Nucleic Acids, triplex formation and bis-PNAs, targeting of double-stranded DNA by Peptide Nucleic Acids, ***antisense*** and antigene expts., and Peptide Nucleic Acids as hybridization probes.
RE.CNT 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 197 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:487381 CAPLUS
DN 131:126414
TI New members of the glypican gene family and the association of mutations with Simpson-Golabi-Behmel overgrowth syndrome
IN Veugelers, Mark Paul Dittmar; David, Guido Joseph Frans
PA Vlaams Interuniversitair Instituut Voor Biotechnologie, Belg.
SO PCT Int. Appl., 79 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9937764 A2 19990729 WO 1999-EP329 19990120 WO 2000037764 A3 20000203 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 9924229 A1 19990809 AU 1999-24229 19990120
PRAI EP 1998-200226 19980127 WO 1999-EP329 19990120
AB The invention relates to a novel polynucleotide encoding a new glypican-related protein (glypican-6) and the gene for glypican-4 as well as derivs. of both genes for use in methods of diagnosis and therapy. Derivs. comprise for example fragments of the gene either isolated or synthetic and having a length that is smaller than the complete gene; primers, comprising .gtoreq.10 consecutive gene specific nucleotides, preferably about 20 gene specific consecutive nucleotides of the nucleotide sequence of the gene; longer oligonucleotides up to the full length of the gene; ***antisense*** variants of the gene, the fragments or the primers; antibodies directed to the gene, fragments, primers or complementary strands thereof; any specific ligand for DNA that can be used as a specific probe, ***peptide*** ***nucleic*** ***acid*** probes. Glypican-6 and glypican-4 are heparan sulfate proteoglycans 555 and 556 amino acid residues in length, resp. Their genes are localized to human chromosome 13q32 and Xq26, resp. Mutations in these genes and gene products are assocd. with Simpson-Golabi-Behmel overgrowth syndrome, and thus provide reagents for use in diagnosis or therapy. PCR primers/hybridization probes are provided for detecting mutations and/or translocations in the glypican genes, and antibodies may be used in immunoassays.

L9 ANSWER 198 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:461907 CAPLUS
DN 131:224005
TI Peptide nucleic acids as therapeutic agents
AU Nielsen, Peter E.
CS Center for Biomolecular Recognition, Department of Medical Biochemistry and Genetics, Biochemical Laboratory B, The Panum Institute, Copenhagen N, 2200, Germany
SO Current Opinion in Structural Biology (1999), 9(3), 353-357
CODEN: COSBEF; ISSN: 0959-440X
PB Current Biology Publications
DT Journal; General Review
LA English
AB A review with 46 ref. Peptide nucleic acids (PNAs) have been around for more than seven years and it was hoped, at their introduction, that they would quickly enter the fields of ***antisense*** and antigen technol. and drug development. Despite their extremely favorable hybridization and stability properties, as well as the encouraging ***antisense*** and antigen activity of ***PNA*** in cell-free systems, progress has been slow and expts. on cells in culture and in animals have been lacking. Judging from the very promising results published within the past year, however, there is every reason to believe that both ***PNA*** ***antisense*** and, possibly, ***PNA*** antigen research will strongly pick up momentum again. Specifically, it has been demonstrated that certain peptide- ***PNA*** conjugates are taken up very efficiently by, at least some, eukaryotic cells and that ***antisense*** down regulation of target genes in nerve cells in culture is attainable using such ***PNA*** conjugates. Perhaps even more exciting is that ***antisense*** -compatible effects have been reported using PNAs injected into the brain of rats. Finally, it has been shown that the bacterium Escherichia coli is susceptible to ***antisense*** gene regulation using ***PNA*** .
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 199 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:461774 CAPLUS
DN 131:248118
TI Peptide nucleic acids targeted to the neurotensin receptor and administered i.p. cross the blood-brain barrier and specifically reduce gene expression
AU Tyler, Beth M.; Jansen, Karen; McCormick, Daniel J.; Douglas, Christopher L.; Boules, Mona; Stewart, Jennifer A.; Zhao, Lihong; Lacy, Benjamin; Cusack, Bernadette; Fauq, Abdul; Richelson, Elliott
CS Laboratories of Neuropsychopharmacology, Mayo Foundation for Medical and Educational Research, Jacksonville, FL, 32224, USA

SO Proceedings of the National Academy of Sciences of the United States of America (1999), 96(12), 7053-7058 CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB I.p. injection of an unmodified ***antisense*** ***peptide*** ***nucleic*** ***acid*** (***PNA***) complementary to mRNA of the rat neurotensin (NT) receptor (NTR1) was demonstrated by a gel shift assay to be present in brain, thus indicating that the ***PNA*** had in fact crossed the blood-brain barrier. An i.p. injection of this ***antisense*** ***PNA*** specifically inhibited the hypothermic and antinociceptive activities of NT microinjected into brain. These results were assocd. with a redn. in binding sites for NT both in brain and the small intestine. Addnl., the sense-NTR1 ***PNA*** , targeted to DNA, microinjected directly into the brain specifically reduced mRNA levels by 50% and caused a loss of response to NT. To demonstrate the specificity of changes in behavioral, binding, and mRNA studies, animals treated with NTR1 ***PNA*** were tested for behavioral responses to morphine and their mu receptor levels were detd. Both were found to be unaffected in these NTR1 ***PNA*** -treated animals. The effects of both the ***antisense*** and sense PNAs were completely reversible. This work provides evidence that any ***antisense*** strategy targeted to brain proteins can work through i.p. delivery by crossing the normal blood-brain barrier. Equally important was that an antigene strategy, the sense ***PNA*** , was shown in vivo to be a potentially effective therapeutic treatment.
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 200 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:376918 CAPLUS
DN 131:157957
TI Modular Nucleic Acid Surrogates. Solid Phase Synthesis of .alpha.-Helical Peptide Nucleic Acids (.alpha.PNAs)
AU Garner, Philip; Dey, Subhakar; Huang, Yumei; Zhang, Xiao
CS Department of Chemistry, Case Western Reserve University, Cleveland, OH, 44106-7078, USA
SO Organic Letters (1999), 1(3), 403-405 CODEN: ORLEF7; ISSN: 1523-7060
PB American Chemical Society
DT Journal
LA English
AB The synthesis and characterization of prototype .alpha.-helical ***peptide*** ***nucleic*** ***acid*** (.alpha. ***PNA***) modules, e.g., Ac-C(Acm)-G-ST-D-A-E-ST-A-A-K-ST-A-A-E-ST-A-Aib-A-ST-K-G- NH2 [1; Acm = acetamidomethyl, ST = 1-[(Ser)methyl]thymine residue, Aib = 2-aminoisobutyric acid residue] as well as disulfide dimers are reported. These mols. combine an .alpha.-helical peptidyl scaffold with well-defined nucleobase mol. recognition patterns and could serve as a basis for novel ***antisense*** and/or antigene agents. Structure assignments for these .alpha.PNAs were supported by MALDI-TOF mass spectrometry, and the .alpha.-helical nature of 1 dimer in water was confirmed by CD spectroscopy.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 201 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:360133 CAPLUS
DN 131:179480
TI Modified peptide nucleic acids are internalized in mouse macrophages RAW 264.7 and inhibit inducible nitric oxide synthase
AU Scarfi, Sonia; Giovine, Marco; Gasparini, Anna; Damonte, Gianluca; Millo, Enrico; Pozzolini, Marina; Benatti, Umberto
CS Viale Benedetto XV, Biochemistry Section, Department of Experimental Medicine, University of Genoa, Genoa, 16132, Italy
SO FEBS Letters (1999), 451(3), 264-268 CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English
AB Overexpression of inducible nitric oxide synthase causes the prodn. of high levels of nitric oxide, which, under pathol. conditions, leads to immunosuppression and tissue damage. The results recently obtained using peptide nucleic acids, rather than traditional oligonucleotides as antigen and ***antisense*** mols., prompted us to test their efficacy in the regulation of nitric oxide prodn., thereby overcoming the obstacle of cellular internalization. The cellular permeability of four inducible nitric oxide synthase ***antisense*** peptide nucleic acids of different lengths was evaluated. These peptide nucleic acids were covalently linked to a hydrophobic peptide moiety to increase internalization and to a tyrosine to allow selective 125I radiolabelling. Internalization expts. showed a 3-25-fold increase in the membrane permeability of the modified peptide nucleic acids with respect to controls. inducible nitric oxide synthase inhibition expts. on intact stimulated macrophages RAW 264.7 after passive permeation of the two ***antisense*** peptide nucleic acids 3 and 4 demonstrated a significant decrease (43-44%) in protein enzymic activity with respect to the controls. These data offer a basis for developing a good alternative to conventional drugs directed against inducible nitric oxide synthase overexpression.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 202 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:353234 CAPLUS
DN 131:130246
TI ***Peptide*** ***nucleic*** ***acid*** with ether linkages in the main chain. Synthesis and sequence-specific interaction with DNA
AU Sisido, Masahiko; Arimitsu, Miki; Kuwahara, Masayasu
CS Department of Bioscience and Biotechnology, Faculty of Engineering, Okayama University, Okayama, 700-8530, Japan
SO Peptide Science (1999), Volume Date 1998, 35th, 97-100 CODEN: PSCIFQ; ISSN: 1344-7661
PB Protein Research Foundation
DT Journal
LA English
AB Peptide nucleic acids that have a [NH-C*H(CH2-CH2-CH2-Base)-CH2-O-CH2-CO] monomer unit (oxy-PNAs = OPNAs) with adenine and other nucleobases, were synthesized. The OPNAs have an ether linkage in each monomer unit that improves water soly. and affords sufficient rotational freedom to achieve stable hybridization with nucleic acids. The melting curve of the OPNA(A12)-DNA(T12) complex showed a very sharp transition at Tm=43.degree.C. The transition was much more sharp than that of the corresponding DNA(A12)-DNA(T12) complex, indicating that the OPNA is flexible enough to take nearly optimized double-stranded structure with the complementary DNA. The sharp transition and the improved water soly. make the OPNA a promising ***antisense*** mol. for medicinal and diagnostic uses.
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 203 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:290595 CAPLUS

DN 131:59111
TI Peptide nucleic acids and their phosphonate analogues: synthesis and hybridization properties
AU Efimov, V. A.; Buryakova, A. A.; Choob, M. V.; Chakhmakhlcheva, G.
CS Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, Moscow, 117871, Russia
SO Bioorganicheskaya Khimiya (1998), 24(9), 696-709 CODEN: BIKHD7; ISSN: 0132-3423
PB MAIK Nauka
DT Journal
LA Russian
AB The synthesis of a series of DNA mimics (peptide nucleic acids, phosphonate analogs of peptide nucleic acids, and their hybrids) is described. The preparative synthesis of the corresponding monomers and the solid phase automated synthesis of oligomers-mimics are developed. Modified phosphonate analogs of peptide nucleic acids, in particular chiral derivs. and those with addnl. hydroxyl groups in the side chains of the backbone as well as pyrene derivs. of peptide nucleic acids and their phosphonate analogs, are prepd. The ability of the resulting oligomers specifically to hybridize to DNA and RNA complementary chains is studied. It is shown that phosphonate analogs of peptide nucleic acids and their hybrids with peptide nucleic acids can form complexes with the DNA and RNA complementary strands, the stability of the complexes increasing in parallel with the increase in the no. of ***peptide*** ***nucleic*** ***acid*** residues in the chain of the mimic. This property, along with good water soly., provides the precondition for further evaluation of these compds. as ***antisense*** and antigene agents.

L9 ANSWER 204 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:282231 CAPLUS
DN 130:307520
TI Extracellular administration of polyamide nucleic acid oligomers engenders target-specific biological responses
IN Richelson, Elliott; Tyler, Beth Marie; McCormick, Daniel J.; Cusack, Bernadette Marie; Hoshall, Clark V.; Douglas, Christopher Lee; Jansen, Karen
PA Mayo Foundation for Medical Education and Research, USA
SO PCT Int. Appl., 116 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9920643 A1 19990429 WO 1998-US21888 19981016 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG US 6472209 B1 20021029 US 1997-953269 19971017 US 2003100519 A1 20030529 US 1998-168791 19981008 CA 2306731 AA 19990429 CA 1998-2306731 19981016 AU 9910940 A1 19990510 AU 1999-10940 19981016 AU 741246 B2 20011129 EP 1042349 A1 20001011 EP 1998-953610 19981016 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI BR 9814866 A 20011120 BR 1998-14866 19981016 JP 2003523307 T2 20030805 JP 2000-516984 19981016 MX 200003764 A 20001027 MX 2000-3764 20000417
PRAI US 1997-953269 A 19971017 US 1998-16685 A 19980130 US 1998-168519 A 19981008 US 1998-168714 A 19981008 US 1998-168791 A 19981008 WO 1998-US21888 W 19981016
AB Methods of treating living cells with polyamide nucleic acid (***PNA***) oligomers such that the oligomers cross a biol. barrier and engender a biol. response are disclosed. The invention is based on the observation that extracellularly administered PNAs cross biol. barriers and elicit a sequence-specific biol. response in living cells. Use of PNAs for identifying the function of proteins and of detg. the relative turnover rate of functional proteins is disclosed. Thus, intracranial or peritoneal injection as well as oral administration of ***antisense*** NTR1 neurotensin receptor ***PNA*** oligomer (i.e., NTR1 mRNA-complementary ***PNA***) reduced neurotensin responsiveness in the brains of mice as evidenced by the failure of neurotensin to induce anti-nociception and hypothermia. It appears, therefore, that the PNAs are capable of crossing the blood-brain barrier. The reduced neurotensin responsiveness correlated with a redn. in NTR1 protein as evidenced by redn. in [125I]neurotensin binding. Similar expts. were performed with mu-1 morphine receptor and serotonin receptor ***antisense*** PNAs. Expts. with sense NTR1 neurotensin receptor ***PNA*** oligomer (NTR1 DNA template-complementary ***PNA***) produced results similar to the ***antisense*** NTR1 ***PNA*** , i.e., reduced neurotensin responsiveness. These reduced responsiveness correlated with reduced intracellular NTR1 mRNA levels.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 205 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:235768 CAPLUS
DN 131:19274
TI 2',5'-oligoadenylate-peptide nucleic acids (2-5A-PNAs) activate RNase L
AU Verheijen, Jeroen C.; Van der Marel, Gijsbert A.; Van Boom, Jacques H.; Bayly, Suzanne F.; Player, Mark R.; Torrence, Paul F.
CS Gorlaeus Laboratories, Leiden Institute of Chemistry, Leiden, 2300 RA, Neth.
SO Bioorganic & Medicinal Chemistry (1999), 7(3), 449-455 CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
AB To potentiate the 2-5A (2',5'-oligoadenylate)-***antisense*** and ***peptide*** ***nucleic*** ***acid*** (***PNA***) approaches to regulation of gene expression, composite mols. were generated contg. both 2-5A and ***PNA*** moieties. 2-5A- ***PNA*** adducts were synthesized using solid-phase techniques. Highly cross-linked polystyrene beads were functionalized with glycine tethered through a p-hydroxymethyl-benzoic acid linker and the ***PNA*** domain of the chimeric oligonucleotide analog was added by sequential elongation of the amino terminus with the monomethoxytrityl protected N-(2-aminoethyl)-N-(adenin-1-ylacetyl)glycinate. Transition to the 2-5A domain was accomplished by coupling of the ***PNA*** chain to dimethoxytrityl protected N-(2-hydroxyethyl)-N-(adenin-1-ylacetyl)glycinate. Finally, (2-cyanoethyl)-N,N-diisopropyl-4-O-(4,4- dimethoxytrityl)butyl-phosphoramidite and the corresponding (2-cyanoethyl)-N,N-diisopropylphosphoramidite of 5-O-(4,4'- dimethoxytrityl)-3-O-(tert-butyldimethylsilyl)-N6-benzoyl-adenosine were the synthons employed to add the 2 butanediol phosphate linkers and the four 2',5'-linked riboadenylates. The 5'-phosphate moiety was introduced with 2-[[2-(4,4'-dimethoxytrityloxy)ethyl]sulfonyl]ethyl-(2-cyanoethyl)-N,N-diisopropylphosphoramidite. Deprotection with methanolic NH3 and tetraethylammonium fluoride afforded the desired products, 2-5A-pnaA4, 2-5A-pnaA8 and 2-5A-pnaA12. When evaluated for their ability to cause the degrdn. of two different

RNA substrates by the 2-5A-dependent RNase L, these new 2-5A-***PNA*** conjugates were found to be potent RNase L activators. The union of 2-5A and ***PNA*** presents fresh opportunities to explore the biol. and therapeutic implications of these unique approaches to ***antisense*** .
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 206 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:139953 CAPLUS
DN 130:193625
TI Cloning of cDNA for cell cycle-regulating protein AIM-1 and use of AIM-1 as therapeutic agent
IN Tatsuka, Masaaki; Terada, Yasuhiko
PA Chugai Seiyaku Kabushiki Kaisha, Japan
SO PCT Int. Appl., 44 pp. CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9909160 A1 19990225 WO 1998-JP3641 19980817 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 9886496 A1 19990308 AU 1998-86496 19980817 JP 11164694 A2 19990622 JP 1998-246568 19980817 EP 1004667 A1 20000531 EP 1998-937837 19980817 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI JP 1997-235371 19970815 WO 1998-JP3641 19980817
OS CASREACT 130:193625
AB The gene encoding AIM-1 (aurora and IPL-1 like midbody-assocd. protein kinase) is isolated from the log phase of the cultured NHK-49F rat cells using the primers derived from the serine-threonine kinase domain and the entire protein sequence deduced. The mRNA of AIM-1 is detectable from the late S phase and reaches the peak in the G2-M phase. Northern blot anal. shows AIM-1 is highly expressed in testis, spleen, and lung tissues. Cloning of cDNA for AIM-1 from human HeLa cells is also described (sequences not given). Claimed are methods of recombinant prepn. of the protein, AIM-1 expression-inhibiting ***antisense*** oligonucleotides or peptide nucleic acids (***PNA***), antibodies to AIM-1, and (antitumor) therapeutics contg. AIM-1 inhibitors such as AIM-1(K-R), AIM-1 protein phosphorylation inhibitors, or antibodies. Methods of screening serine-threonine kinase inhibitors using AIM-1 gene or protein are also claimed.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 207 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:124044 CAPLUS
DN 130:293396
TI Applications of peptide nucleic acids
AU Nielsen, Peter
CS Center for Biomolecular Recognition, Department of Medical Biochemistry and Genetics, Biochemical Laboratory B, The Panum Institute, Copenhagen, 2200, Den.
SO Current Opinion in Biotechnology (1999), 10(1), 71-75
CODEN: CUOBE3; ISSN: 0958-1669
PB Current Biology Publications
DT Journal; General Review
LA English
AB A review with 47 refs. Several exciting new developments in the applications of the DNA mimic ***peptide*** ***nucleic*** ***acid*** (***PNA***) have been published recently. A possible breakthrough may have come in efforts to develop ***PNA*** into gene therapeutic drugs. In eukaryotic systems, ***antisense*** activity of PNAs (as peptide conjugates) has been reported in nerve cells and even in rats upon injection into the brain, and ***antisense*** activity has also been demonstrated in Escherichia coli. ***PNA*** hybridization technol. has developed rapidly with in situ hybridization, and exciting new methods based on MALDI-TOF detection have also been presented.
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 208 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:96382 CAPLUS
DN 130:163975
TI Conjugates of transporter peptides and nucleic acid analogs for improved delivery of ***antisense*** constructs
IN Langel, Ulo; Bartfai, Tamas; Pooga, Margus; Valkna, Andres; Saar, Kulliki; Hallbrink, Mattias
PA The Perkin-Elmer Corporation, USA
SO PCT Int. Appl., 61 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9905302 A1 19990204 WO 1998-US14761 19980716 W: AU, CA, JP RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE AU 9884080 A1 19990216 AU 1998-84080 19980716 AU 741546 B2 20011206 US 6025140 A 20000215 US 1998-116294 19980716 EP 998577 A1 20000510 EP 1998-934592 19980716 R: CH, DE, FR, GB, IT, LI, SE JP 2002511885 T2 20020416 JP 1999-509910 19980716
PRAI US 1997-53678P P 19970724 WO 1998-US14761 W 19980716
OS MARPAT 130:163975
AB Constructs of peptides and nucleic acid analogs conjugated together for transport across a lipid membrane and for delivery into interactive contact with intracellular polynucleotides are disclosed. Transport is effected through at least the exterior membrane of a cell, and most likely also through the walls of subcellular structures sepd. from the cytosol by lipid membranes, including the nucleus, mitochondria, ribosomes, etc. ***Peptide*** ***nucleic*** ***acid*** (***PNA***) analog sequences conjugated through a labile disulfide bond to transporting peptides, are intracellularly cleaved, and target mRNA (antigene) or dsDNA (***antisense***). Such conjugates may be used for selective inhibition of transcription, translation, RNA or DNA expression, DNA replication, and DNA or RNA regulatory functions. Thus, a ***PNA*** ***antisense*** to the human type 1 galanin receptor is linked via a labile cysteine disulfide bond to biotin-labeled peptides known to import cell membrane permeant properties, i.e., transportan [galanin(1-12)-Lys- mastoparan(1-14)amide] or pAntennapedia [pAntp(43-58), the third helix of Atennapedia homeodomain]. The resulting conjugates demonstrate improved internalization and down-regulate the human galanin receptor in Bowes cell line and in rat spinal cord in vivo.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 209 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:91165 CAPLUS
TI Minimal modification of ***antisense*** oligonucleotides
AU Uhlmann, E.

CS Chemical Research, Hoechst Marion Roussel, Frankfurt, 65926, Germany
SO Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), CARB-005 Publisher: American Chemical Society, Washington, D. C. CODEN: 67GHA6
DT Conference; Meeting Abstract
LA English
AB Uniformly phosphorothioate (PS) modified oligodeoxynucleotides (ODN) are ***antisense*** agents of the first generation. Although a no. of PS-ODN are in advanced stages of clin. development and the first ***antisense*** drug (Vitravene; Isis Pharmaceuticals) has been approved by the FDA, certain limitations of PS-ODN have emerged. Our approach to overcome these limitations is to reduce the no. of PS linkages within the ODN to a min. which is necessary to stabilize against nucleotlytic degrdn. We have developed a novel protection strategy which is a combination of the end-capping technique and the PS protection of internal pyrimidine positions which are the major sites of endonuclease degrdn. This protection scheme has successfully been used for specific inhibition of expression of various genes. Advantageously, it can also be combined with secondary modifications at the carbohydrate moieties, such as 2'-O-alkyl-modifications, or with partial replacement of the sugar phosphate backbone by 2-aminoethylglycine-based ***PNA*** units (***peptide*** ***nucleic*** ***acid***) leading to DNA- ***PNA*** chimeras.

L9 ANSWER 210 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:91164 CAPLUS
TI Targeting bacterial genes by ***PNA*** ***antisense***
AU Nielsen, Peter E.
CS Center for Biomolecular Recognition, University of Copenhagen, Den.
SO Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), CARB-004 Publisher: American Chemical Society, Washington, D. C. CODEN: 67GHA6
DT Conference; Meeting Abstract
LA English
AB The DNA mimic ***PNA*** (***peptide*** ***nucleic*** ***acid***) is a potential lead for 3rd generation gene therapeutic ***antisense*** and antigene drugs. Recent results showed that genes of the bacteria E.coli can be efficiently down regulated by ***PNA*** ***antisense*** , thereby suggesting a road towards genetic antibacterial drugs. This talk will discuss progress in this area with special attention to cellular uptake of ***PNA*** .

L9 ANSWER 211 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:64975 CAPLUS
DN 130:134948
TI ***PNA*** probes and surface plasmon resonance for detecting DNA
IN Karube, Isao; Sawata, Shinya; Nagata, Ryohei
PA Dai Nippon Printing Co., Ltd., Japan
SO PCT Int. Appl., 39 pp. CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9902730 A1 19990121 WO 1998-JP3077 19980709 W: US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE JP 11332595 A2 19991207 JP 1998-141433 19980522 EP 950718 A1 19991020 EP 1998-931022 19980709 R: DE, FR, GB, IT US 2003165953 A1 20030904 US 2003-334831 20030102 PRAI JP 1997-183710 A 19970709 JP 1998-75350 A 19980324 JP 1998-141433 A 19980522 WO 1998-JP3077 W 19980709 US 1999-147791 B2 19990309 US 2000-749998 B1 20001229
AB Disclosed is a PCR-based method for detecting a target DNA sequence by a hybridization procedure using ***PNA*** (***peptide*** ***nucleic*** ***acid***) probes to replace the conventional DNA probes. The degree of hybridization is detd. by surface plasmon resonance (SPR). The method reduces the influences of the salt concn. during signal detection and thus improves the sensitivity. The ***PNA*** probes may also be immobilized on the detector tips of SPR. Detection of pathogen Escherichia coli strain O-157 and other toxin-producing pathogens by this method was demonstrated.
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 212 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:26690 CAPLUS
DN 130:204715
TI Modified (***PNA*** , 2'-O-methyl and phosphoramidate) anti-TAR ***antisense*** oligonucleotides as strong and specific inhibitors of in vitro HIV-1 reverse transcription
AU Boulme, Florence; Freund, Frederic; Moreaul, Serge; Nielsen, Peter E.; Gryaznov, Sergei; Toulme, Jean-Jacques; Litvak, Simon
CS CNRS-Universite Victor Segalen Bordeaux, Bordeaux, 33077, Fr.
SO Nucleic Acids Research (1998), 26(23), 5492-5500 CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB Natural 3-phosphodiester 16mer and 15mer ***antisense*** oligonucleotides targeted against the HIV-1 and HIV-2 TAR RNAs, resp., were previously described as sequence-specific inhibitors of in vitro retroviral reverse transcription. In this work, we tested chem. modified oligonucleotide analogs: .alpha.-phosphodiester, phosphorothioate, methylphosphonate, ***peptide*** ***nucleic*** ***acid*** or ***PNA*** , 2'-O-Me and (N3'-P5') phosphoramidate versions of the 16mer anti-TAR oligonucleotide. ***PNA*** , 2'-O-Me and (N3'-P5') phosphoramidate oligomers showed a strong inhibitory effect compared with the unmodified 16mer, with reverse transcription inhibition (IC50) values in the nanomolar range. The inhibition was sequence-specific, as scrambled and mismatched control oligonucleotides were not able to inhibit cDNA synthesis. No direct binding of the 2'-O-Me, ***PNA*** or (N3'-P5') phosphoramidate anti-TAR oligonucleotides to the HIV-1 reverse transcriptase was obsd. The higher Tm obtained with 2'-O-Me, (N3'-P5') phosphoramidate and ***PNA*** mols. concerning the annealing with the stem-loop structure of the TAR RNA, in comparison with the .beta.-phosphodiester oligonucleotides, is correlated with their high inhibitory effect on reverse transcription.
RE.CNT 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 213 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:9992 CAPLUS
DN 130:81891
TI Preparation of peptido oligonucleotides (PONs) and their combinatorial libraries as ***antisense*** agents for treatment of gene-related diseases
IN Cole, Ryszard; Liu, Weiguo
PA The University of North Carolina At Chapel Hill, USA
SO PCT Int. Appl., 59 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9858256 A1 19981223 WO 1998-US12580 19980615 W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,

CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG AU 9881477 A1 19990104 AU 1998-81477 19980615
PRAI US 1997-49634P P 19970616 WO 1998-US12580 W 19980615
OS MARPAT 130:81891
AB The present invention provides for libraries of nucleotide-like substances S-(pX-AA)n-Y (S = H, linker, modifying group, peptide residue; Y = Y, linker, modifying group, amino acid residue, peptide residue; AA = natural or unnatural amino acid residue excluding pX; pX = optically active amino acid nucleoside residue H2NCH(CH2CH2X)CO2H; X = nucleobase residue or deriv. thereof, including thymine, cytosine, uracil, adenine, and guanine; n .gtoreq. 1), referred to as peptido oligonucleotides (PONs). The PONs of this invention consist of natural and unnatural D-or L-amino acids, purine or pyrimidine derived nucleobases, and a 4 carbon chain connecting the nucleobases and the amino acids together through amide linkages to form a peptide backbone. Thus, PON H-Lys-(pT-Gly)10-Gly-NH2 (pT = thymine-contg. amino acid residue I) (prepn. given) showed recognition of deoxyadenosine 12-mer (dA)12 in a thermal denaturation study.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 214 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:788695 CAPLUS
DN 130:48274
TI Assaying nucleic acids in solution using a fluorescent intensity quenching effect with ***antisense*** ***peptide*** ***nucleic*** ***acid*** probes
IN Wu, Yuan Min; Nie, Eileen Xiao-Feng
PA Lorne Park Research, Inc., Can.
SO U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 807,901. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI US 5846729 A 19981208 US 1997-886280 19970701 ZA 9801660 A 19990125 ZA 1998-1660 19980227 US 6046004 A 20000404 US 1998-83410 19980522 US 6251591 B1 20010626 US 1998-83837 19980522 WO 9901578 A1 19990114 WO 1998-IB1016 19980630 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG AU 9880302 A1 19990125 AU 1998-80302 19980630 AU 730865 B2 20010315 EP 1002125 A1 20000524 EP 1998-928474 19980630 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI JP 2001510681 T2 20010807 JP 2000-501276 19980630 ZA 9805758 A 19990127 ZA 1998-5758 19980701
PRAI US 1997-807901 A2 19970227 US 1997-870370 A2 19970606 US 1997-886280 A2 19970701 WO 1998-IB1016 W 19980630
AB The invention provides a method for rapidly, economically and efficiently sequencing and assaying nucleic acids in a liq. medium using laser-induced fluorescence of ***antisense*** probes, including ***PNA*** probes. Fluorescent intensity of the resulting medium is inversely proportional to the hybridization efficiency of the probes with respect to the target sequence. The method is particularly advantageous in not requiring sepn. of unhybridized probes and hybridization complexes prior to detection. The method can be used to identify accessible regions in folded nucleotide sequences, to det. the no. of mismatched pairs in a hybridization complex, and to map genomes.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 215 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:761904 CAPLUS
DN 130:4030
TI Preparation of peptide nucleic acids using 4-component Ugi addition reaction
IN Domling, Alexander; Richter, Wolfgang
PA Morphochem G.m.b.H., Germany
SO PCT Int. Appl., 59 pp. CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9851697 A2 19981119 WO 1998-EP2860 19980514 WO 9851697 A3 19990514 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG DE 19720216 A1 19981119 DE 1997-19720216 19970514 DE 19720165 A1 19990128 DE 1997-19720165 19970514 AU 9880175 A1 19981208 AU 1998-80175 19980514 AU 750974 B2 20020801 EP 983290 A1 20000308 EP 1998-928268 19980514 R: CH, DE, DK, ES, FR, GB, IT, LI, SE JP 2002500643 T2 20020108 JP 1998-548814 19980514 US 6355726 B1 20020312 US 1999-423594 19991110 NO 9905551 A 20000112 NO 1999-5551 19991112
PRAI DE 1997-19720165 A 19970514 DE 1997-19720216 A 19970514 WO 1998-EP2860 W 19980514
AB The invention relates to a method for producing polymers having nucleo-bases as side groups (peptide nucleic acids) by means of multi-component reactions, esp. the Ugi reaction. By virtue of the multi-constituent nature of prodn., the properties of the polymers can be varied to a greater degree than before and can be adapted to meet the requirements for use as ***anti*** - ***sense*** or antigen therapeutic agent or diagnostic reagent. Thus, a 4-component Ugi addn. reaction using 1-isocyano-3-N(tert-butoxy-carbonyl)propane, paraformaldehyde, benzylamine, and N-(4-methoxy-benzoyl)-N9-adenine acetic acid as, resp., the isocyanide, oxo, amine, and acid components, gave (I).

L9 ANSWER 216 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:746367 CAPLUS
DN 130:119798
TI A ***peptide*** ***nucleic*** ***acid*** (***PNA***) is more rapidly internalized in cultured neurons when coupled to a retro-inverso delivery peptide. The ***antisense*** activity depresses the target mRNA and protein in magnocellular oxytocin neurons
AU Aldrian-Herrada, Gudrun; Desarmenien, Michel G.; Orcel, Helene; Boissin-Agasse, Line; Mery, Jean; Brugidou, Jean; Rabie, Alain
CS CNRS-UPR 1086, CRBM, Montpellier, 34033, Fr.

SO Nucleic Acids Research (1998), 26(21), 4910-4916 CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB A ***peptide*** ***nucleic*** ***acid*** (***PNA***) ***antisense*** for the AUG translation initiation region of prepro-oxytocin mRNA was synthesized and coupled to a retro-inverso peptide that is rapidly taken up by cells. This bioconjugate was internalized by cultured cerebral cortex neurons within minutes, according to the specific property of the vector peptide. The ***PNA*** alone also entered the cells, but more slowly. Cell viability was unaffected when the ***PNA*** concns. were lower than 10 .mu.M and incubation times less than for 24 h. Magnocellular neurons from the hypothalamic supraoptic nucleus, which produce oxytocin and vasopressin, were cultured in chem. defined medium. Both ***PNA*** and vector peptide-***PNA*** depressed the amts. of the mRNA coding for prepro-oxytocin in these neurons. A scrambled ***PNA*** had no effect and the very cognate prepro-vasopressin mRNA was not affected. The ***antisense*** ***PNA*** also depressed the immunocytochem. signal for prepro-oxytocin in this culture in a dose- and time-dependent manner. These results show that PNAs driven by the retro-inverso vector peptide are powerful ***antisense*** reagents for use on cells in culture.
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 217 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:618936 CAPLUS
DN 129:227036
TI Peptide nucleic acids (***PNA***) and ***PNA*** -DNA chimeras. From high binding affinity towards biological function
AU Uhlmann, Eugen
CS Hoechst Marion Roussel Deutschland G.m.b.H., Frankfurt/Main, D-65926, Germany
SO Biological Chemistry (1998), 379(8/9), 1045-1052 CODEN: BICHF3; ISSN: 1431-6730
PB Walter de Gruyter & Co.
DT Journal; General Review
LA English
AB A review is given with 45 refs. Oligonucleotide analogs are of major interest as tools in mol. biol., as diagnostics, and as potential pharmaceuticals which bind in a predictable way to certain nucleic acid target sequences, aiming at the inhibition of expression of disease-causing genes. One of the most promising nucleic acid mimetics are the peptide- or polyamide- nucleic acids (***PNA***) which bind with higher affinity to DNA and RNA than natural oligonucleotides. In these non-ionic PNAs, the entire sugar-phosphate backbone is replaced by an N-amino-ethylglycine-based polyamide structure. A unique property of ***PNA*** is its ability to displace one strand of a DNA double-helix. This strand displacement process, which is inefficient with DNA, is supported by the formation of an unusually stable internal (***PNA***), DNA triple helix. The combination of ***PNA*** and DNA in 1 mol. results in ***PNA*** /DNA chimeras with new properties. They show improved aq. soly. compared to pure PNAs due to their partially neg. charged structure. The cellular uptake of the chimeras is better than of pure PNAs. In contrast to ***PNA*** , the chimeras bind exclusively in the antiparallel orientation under physiol. conditions. The binding affinity is generally stronger when the ***PNA*** /DNA chimeras are hybridized to RNA than to DNA, whereby the strength of binding strongly depends on the ***PNA*** : DNA ratio. ***PNA*** /DNA chimeras are recognized as substrates by various nucleic acid processing enzymes, and consequently can also assume biol. functions, such as a primer function for DNA polymerases. Pure ***PNA*** cannot induce RNase H cleavage of target RNA, which is believed to support the biol. efficacy of ***antisense*** agents. DNA-***PNA*** chimeras are able to stimulate cleavage of the target RNA by RNase H upon formation of an RNA chimera duplex.

L9 ANSWER 218 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:591772 CAPLUS
DN 129:310817
TI Cell penetrating ***PNA*** constructs regulate galanin receptor levels and modify pain transmission in vivo
AU Pooga, Margus; Soomets, Ursel; Hallbrink, Mattias; Valkna, Andres; Saar, Kulliki; Rezaei, Khadijeh; Kahl, Ulrika; Hao, Jing-Xia; Xu, Xiao-Jun; Wisenfeld-Hallin, Zsuzsanna; Hokfelt, Tomas; Bartfai, Tamas; Langel, Ulo
CS Dep. Neurochemistry and Neurotoxicology, Arrhenius Labortories, Stockholm Univ., Stockholm, S-10691, Swed.
SO Nature Biotechnology (1998), 16(9), 857-861 CODEN: NABIF9; ISSN: 1087-0156
PB Nature America
DT Journal
LA English
AB Peptide nucleic acids (PNAs) form stable and tight complexes with complementary DNA and/or RNA and would be promising ***antisense*** reagents if their cellular delivery could be improved. We show that a 21-mer ***PNA*** , complementary to the human galanin receptor type 1 mRNA, coupled to the cellular transporter peptides, transportan or Antennapedia(43-58), is efficiently taken up into Bowes cells where they block the expression of galanin receptors. In rat, the intrathecal administration of the peptide- ***PNA*** construct results in a decrease in galanin binding in the dorsal horn. The decrease in binding results in the inability of galanin to inhibit the C fibers stimulation-induced facilitation of the rat flexor reflex, demonstrating that peptide- ***PNA*** constructs act in vivo to suppress expression of functional galanin receptors.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 219 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:575505 CAPLUS
DN 129:327320
TI Peptide nucleic acids
AU Nielsen, Peter E.
CS Center for Biomolecular Recognition Panum Institute, University of Copenhagen, Den.
SO Science & Medicine (Philadelphia) (1998), 5(5), 48-55 CODEN: SCMEFJ; ISSN: 1087-3309
PB Science & Medicine
DT Journal; General Review
LA English
AB A review, with 5 refs., of the author's development of the ***PNA*** mol. and its uses. Synthetic mols. that mimic DNA but are more stable might substitute for DNA in diagnostic and therapeutic applications. Such a mol. is ***peptide*** ***nucleic*** ***acid*** , which was designed as a reagent for sequence-specific recognition of double-stranded DNA. As the properties of this DNA mimic have been unraveled over the past seven years, a wider range of uses has become apparent. Peptide nucleic acids have a no. of advantages over DNA as hybridization probes in genetic detection, and they should be more suitable than DNA for ***antisense*** and anti-gene therapeutic agents. Inefficient uptake of peptide nucleic acids by cells is an obstacle that may be overcome by linking ***PNA*** 's to peptides.

L9 ANSWER 220 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1998:543690 CAPLUS
DN 129:280795
TI Drug delivery of ***antisense*** molecules to the brain for treatment of Alzheimer's disease and cerebral AIDS
AU Boado, Ruben J.; Tsukamoto, Haruhisa; Pardridge, William M.
CS Department of Medicine, UCLA School of Medicine, Los Angeles, CA, 90095, USA
SO Journal of Pharmaceutical Sciences (1998), 87(11), 1308-1315 CODEN: JPMSAE; ISSN: 0022-3549
PB American Chemical Society
DT Journal; General Review
LA English
AB A review with 69 refs. ***Antisense*** oligonucleotides (ODNs) and peptide nucleic acids (PNAs) are potential therapeutics for eradication of malignancies, viral infections, and other pathologies. However, ODNs and PNAs in general are unable to cross cellular membranes and blood-tissue barriers, such as the blood-brain barrier (BBB), which is only permeable to lipophilic mols. of mol. wt. <600 Da. Cellular delivery systems based on conjugates of streptavidin (SA) and the OX26 monoclonal antibody directed to the transferrin receptor may be employed as a universal carrier for the transport of mono-biotinylated peptides, ODNs, or PNAs. 3'-Biotinylation of phosphodiester (PO)-ODN produces complete protection of ODN against serum and cellular 3'-exonucleases, facilitating the conjugation to avidin-based delivery systems and maintaining the activation of RNase H. These delivery systems markedly increased the cellular uptake and ***antisense*** efficacy of 3'-biotinylated ODNs in models of Alzheimer's disease and HIV-AIDS. In vivo brain delivery studies demonstrated that 3'-protected PO-ODNs and PO-phosphorothioate(PS)- ODN hybrids contg. a single PO linkage are subjected to endonuclease degrdn. in vivo. On the contrary PS-ODNs, which were also protected at 3'-terminus by biotinylation, are metabolically stable in vivo and resistant to exo/endonuclease degrdn. However, because of the strong binding of these oligomers to plasma protein, PS-ODNs are poorly transported into the brain through the BBB by the OX26-SA delivery vector following i.v. administration. PNAs are also resistant to exo/endonuclease and protease degrdn., and these mols. biotinylated at the amino terminal group were transported into the brain by the OX26-SA delivery system with brain uptake levels comparable to that of morphine. Using the rev gene of HIV as a model target, RNase protection assays and cell-free translation arrest showed that the ***PNA*** -OX26-SA conjugate maintained active recognition and inactivation of target mRNA, resp. The overall exptl. evidence suggests that ***PNA*** -OX26-SA conjugates represent optimal ***antisense*** mols. for drug delivery to the brain.
RE.CNT 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 221 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:534922 CAPLUS
DN 129:175921
TI Preparation of oligodeoxyribonucleotides as ***antisense*** inhibitors of ICAM-1, E-selectin, and HCMV IE1/IE2
IN Baker, Brenda; Bennett, C. Frank; Anderson, Kevin P.
PA Isis Pharmaceuticals, Inc., USA
SO U.S., 15 pp., Cont.-in-part of U.S. Ser. No. 440,740. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 22 PATENT NO. KIND DATE APPLICATION NO. DATE ---
PI US 5789573 A 19980804 US 1996-653653 19960524 US 5591720 A 19970107 US 1992-927506 19921119 US 5591623 A 19970107 US 1993-7997 19930121 US 5514788 A 19960507 US 1993-63167 19930517 US 5843738 A 19981201 US 1995-440740 19950512 WO 9745437 A1 19971204 WO 1997-US7132 19970429 W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG AU 9727474 A1 19980105 AU 1997-27474 19970429 AU 712228 B2 19991104 EP 918787 A1 19990602 EP 1997-921438 19970429 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI JP 11513889 T2 19991130 JP 1997-532955 19970429 US 2002052331 A1 20020502 US 2001-808680 20010315
PRAI US 1990-567286 B2 19900814 US 1990-568366 B2 19900816 US 1992-939855 B2 19920902 US 1992-927506 A2 19921119 US 1993-7997 A2 19930121 US 1993-63167 A2 19930517 US 1995-440740 A2 19950512 WO 1991-US5815 W 19910814 US 1993-969151 B1 19930210 US 1996-653653 A2 19960524 WO 1997-US7132 W 19970429 US 1999-194230 A1 19990224
AB Compns. and methods are provided for inhibiting the translation of a capped target mRNA. ***Antisense*** oligomers of the invention are targeted to the 5' cap region of the target mRNA and include oligodeoxyribonucleotides, PNAs, or oligodeoxyribonucleotides modified at the 2' position of the sugar. Preferably said oligomers inhibit protein translation directly via interference with ribosome assembly.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 222 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:481712 CAPLUS
DN 129:265242
TI ***Antisense*** molecules conjugated to a cellular delivery system inhibit the expression of the HIV-rev protein
AU Boado, R. J.; Tsukamoto, H.; Pardridge, William M.
CS Department of Medicine, UCLA School of Medicine, Los Angeles, CA, 90095, USA
SO Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1998), 25th, 101-102 CODEN: PCRMEY; ISSN: 1022-0178
PB Controlled Release Society, Inc.
DT Journal
LA English
AB ***Antisense*** mols. were monobiotinylated (+bio) and non-biotinylated (-bio) peptide nucleic acids complementary to nucleotides 5980-5997 of the HIV-1 genome, which correspond to the region around the methionine initiation codon of rev mRNA. The efficacy of these ***antisense*** mols. in inactivating the target mRNA was investigated in a translation arrest assay. The rev-mRNA was prepd. by in vitro transcription using a transcription plasmid named BK-rev, which contains the rev cDNA under the T7 RNA polymerase promoter. Both +bio and -bio oligomers were incubated in the presence or absence of the OX26-SA delivery system with 2 .mu.g rev mRNA. Translation was performed in the rabbit reticulocyte lysate with 3H-leucine, and translated products were analyzed by immunopptn. followed by SDS/PAGE and autoradiog. The anti-rev oligomer is able to recognize and inhibit the translation of the rev gene. OX26-SA conjugates are transported into the b rain with levels of brain uptake comparable to that of morphine, suggesting that anti-rev-OX26-SA conjugates may be an optimal formulation for ***antisense*** delivery to the brain.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 223 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1998:427139 CAPLUS
DN 129:183716
TI ***Antisense*** properties of ***peptide*** ***nucleic*** ***acid***
AU Nielsen, P. E.
CS Center for Biomolecular Recognition, Department of Medical Biochemistry and Genetics, Biochemical Laboratory B, The Panum Institute, Copenhagen N, DK-2200, Den.
SO Handbook of Experimental Pharmacology (1998), 131(Antisense Research and Application), 545-560 CODEN: HEPHD2; ISSN: 0171-2004
PB Springer-Verlag
DT Journal; General Review
LA English
AB A review with many refs. The hybridization properties of ***peptide*** ***nucleic*** ***acid*** (***PNA***) combined with its ease of synthesis and high chem. and biol. stability rapidly made this mol. a very attractive lead compd. for the development of ***antisense*** gene therapeutic drugs. Much has been learned about the chem. and biol. properties of ***PNA*** , and the present review discusses these developments in terms of ***antisense*** technol. Although crucial information about the pharmacokinetic properties of ***PNA*** is still lacking and no animal studies in general have yet been reported, the properties unveiled so far by ***PNA*** seem to give reason for optimism regarding the successful development of ***PNA*** -based gene therapeutic agents. Since functional modification of the ***PNA*** -based backbone is feasible, such modifications should allow optimization of the phys. and pharmacol. properties of a given ***PNA*** oligomer with compromising its favorable hybridization properties.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 224 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:407004 CAPLUS
DN 129:175951
TI Comprehensive nomenclature for the fragment ions produced from collisional activation of peptide nucleic acids
AU Flora, Jason W.; Muddiman, David C.
CS Department of Chemistry, Virginia Commonwealth University, Richmond, VA, 23284, USA
SO Rapid Communications in Mass Spectrometry (1998), 12(12), 759-762 CODEN: RCMSEF; ISSN: 0951-4198
PB John Wiley & Sons Ltd.
DT Journal
LA English
AB A relatively new class of DNA mimics, peptide nucleic acids (***PNA*** 's), have generated increasing interest and importance over the last few years. These mols. have a neutral 'peptide-like' backbone granting them many advantageous properties which lead to their potential use as ***antisense*** and antigene therapeutics. Due to the promising properties possessed by ***PNA*** 's, there is a demand for the development of anal. methods for characterization of these mols. The authors have been investigating the gas-phase fragmentation pathways of singly and multiply charged ***PNA*** 's using electrospray ionization in conjunction with Fourier transform ion cyclotron resonance mass spectrometry. Fragmentations induced by sustained off-resonance irradn. and nozzle-skimmer dissocn. have revealed water loss, cleavages of the methylene carbonyl linker (to which the nucleobases are attached), fragmentation along the ***PNA*** backbone, and the elimination of single nucleobases. It is becoming increasingly evident that multi-stage MS is esp. suited to structural characterization of large bio-mols. such as ***PNA*** 's, and herein we propose a comprehensive nomenclature for the product ions produced upon collisional activation of ***PNA*** 's, which is based upon extensive exptl. studies.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 225 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:296358 CAPLUS
DN 129:63699
TI Assessment of high-affinity hybridization, RNase H cleavage, and covalent linkage in translation arrest by ***antisense*** oligonucleotides
AU Gee, Jay E.; Robbins, Ian; Van Der Laan, Alexander C.; Van Boom, Jacques H.; Colombier, Caroline; Leng, Marc; Raible, Annette M.; Nelson, Jeffrey S.; Lebleu, Bernard
CS Institut de Genetique Moleculaire de Montpellier, CNRS, Montpellier, Fr.
SO Antisense & Nucleic Acid Drug Development (1998), 8(2), 103-111 CODEN: ANADF5; ISSN: 1087-2906
PB Mary Ann Liebert, Inc.
DT Journal
LA English
AB ***Antisense*** oligonucleotides (ONs) are designed to hybridize target mRNA in a sequence-specific manner and inhibit gene expression by preventing translation, either by activation of RNase H or steric blockage of the ribosome complex. Second-generation ONs, which possess greater binding affinity for target RNA relative to the isosequential phosphodiester (PO) ONs, have been developed and include, among others, peptide nucleic acids (***PNA***) and N3' .fwdarw. P5' phosphoramidate oligonucleotides (npONs). In the present study, ***PNA*** and npON derivs. were targeted to the coding portion of the complementary mRNA of the N protein of the vesicular stomatitis virus (VSV) in order to evaluate their ability to arrest translation in an in vitro rabbit reticulocyte lysate system. High-affinity hybridization of ONs lacking RNase H activity was not sufficient to block translation in this test system. Only ***antisense*** ONs acting via an RNase H mechanism or by steric hindrance through covalent attachment (via transplatin modification) to the target mRNA were found to definitively arrest translation in this study.
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 226 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:272290 CAPLUS
DN 129:63629
TI Additive ***antisense*** effects of different PNAs on the in vitro translation of the PML/RAR.alpha. gene
AU Mologni, Luca; Lecoutre, Philipp; Nielsen, Peter E.; Gambacorti-Passerini, Carlo
CS Division of Experimental Oncology D, Istituto Nazionale Tumori, Milan, 20133, Italy
SO Nucleic Acids Research (1998), 26(8), 1934-1938 CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB The potential use of ***peptide*** ***nucleic*** ***acid*** (***PNA***) as a sequence-specific inhibitor of RNA translation is investigated in this report. Three different regions of the PML/RAR.alpha. oncogene, including two AUG potential start codons, were studied as targets of translation inhibition by ***antisense*** ***PNA*** in a cell-free system. A ***PNA*** targeted to the second AUG start codon, which was shown previously to be able to suppress in vitro translation from that site completely, was used alone or in combination with another ***PNA*** directed to the first AUG, and a third ***PNA*** within the 5'-untranslated region (5'-UTR) of mRNA.

When used alone, no ***PNA*** was able to completely block the synthesis of the PML/RAR.alpha. protein. The 5'-UTR ***PNA*** was the most potent translation inhibitor when used as single agent. However, a near complete (.ltoreq.90%) specific inhibition of the PML/RAR.alpha. gene was obtained when the three PNAs were used in combination, thus obtaining an additive ***antisense*** effect.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 227 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:251193 CAPLUS
DN 128:321939
TI Preparation of chiral peptide nucleic acids derived from hydroxyproline
IN Lowe, Gordon
PA Isis Innovation Limited, UK; Lowe, Gordon
SO PCT Int. Appl., 72 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9816550 A1 19980423 WO 1997-GB2820 19971013 W: JP, US RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE EP 956297 A1 19991117 EP 1997-945009 19971013 R: DE, ES, FR, GB, IT, NL JP 2001502673 T2 20010227 JP 1998-518106 19971013 US 6403763 B1 20020611 US 1999-284179 19990409 US 2002072586 A1 20020613 US 2001-932862 20010817
PRAI GB 1996-21367 A 19961014 WO 1997-GB2820 W 19971013 US 1999-284179 A3 19990409
OS MARPAT 128:321939
AB Chiral peptide nucleic acids are provided which hybridize strongly with complementary nucleic acids and have potential as antigene and ***antisense*** agents and as tools in mol. biol. Compds. with cis-stereochem. and based on proline and a spacer amino acid have structures I and II [n = 1-200; B = protected or unprotected nucleobase; R = H,optionally substituted alkyl, aralkyl, or heteroaryl; X = e.g. OH; Y = e.g. H]. Thus, ***peptide*** ***nucleic*** ***acid*** oligomer I (n = 10, B = thymin-1-yl, R = H, Y = H, X = Lys-NH2), prepd. from a protected dipeptide monomer by solid-phase methods, complexed with poly(rA) (Tm = 72.degree., 45% hypochromicity), poly(dA) (Tm = 70.degree., 28% hypochromicity), and dA10 (Tm = 61.degree.).
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 228 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:241166 CAPLUS
TI ***PNA*** , ***antisense*** , and antimicrobials
AU Ecker, David J.; Freier, Susan M.
CS Isis Pharmaceuticals, Carlsbad Res. Cent., Carlsbad, CA, 92008, USA
SO Nature Biotechnology (1998), 16(4), 332 CODEN: NABIF9; ISSN: 1087-0156
PB Nature America
DT Journal
LA English
AB Unavailable
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 229 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:240564 CAPLUS
DN 129:2614
TI ***Antisense*** inhibition of gene expression in bacteria by ***PNA*** targeted to mRNA
AU Good, Liam; Nielsen, Peter E.
CS Center for Biomolecular Recognition, IMBG, Department of Biochemistry, Panum Inst., Univ. of Copenhagen, Copenhagen, Den.
SO Nature Biotechnology (1998), 16(4), 355-358 CODEN: NABIF9; ISSN: 1087-0156
PB Nature America
DT Journal
LA English
AB ***Peptide*** ***nucleic*** ***acid*** (***PNA***) is a DNA mimic with attractive properties for developing improved gene-targeted ***antisense*** agents. To test this potential of ***PNA*** in bacteria, PNAs were designed to target the start codon regions of the Escherichia coli .beta.-galactosidase and .beta.-lactamase genes. Dose-dependent and specific gene inhibition was obsd. in vitro using low nanomolar ***PNA*** concns. and in vivo using low micromolar concns. Inhibition was more efficient for a permeable E. coli strain relative to wild-type K-12. The potency of the anti-.beta.-lactamase PNAs was abolished by a six base substitution, and inhibition could be re-established using a ***PNA*** with compensating base changes. ***Antisense*** inhibition of the .beta.-lactamase gene was sufficient to sensitize resistant cells to the antibiotic ampicillin. The results demonstrate gene- and sequence-specific ***antisense*** inhibition in E. coli and open possibilities for ***antisense*** antibacterial drugs and gene function analyses in bacteria.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 230 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:220217 CAPLUS
DN 128:321903
TI Optimization of the binding properties of ***PNA*** -(5')-DNA chimerae
AU van der Laan, A. C.; Havenaar, P.; Oosting, R. S.; Kuyl-Yeheskiely, E.; Uhlmann, E.; van Boom, J. H.
CS Gorlaeus Lab., Leiden Inst. of Chemistry, Leiden, 2300 RA, Neth.
SO Bioorganic & Medicinal Chemistry Letters (1998), 8(6), 663-668 CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB The synthesis and evaluation of ***PNA*** -(5')-DNA chimera contg. either a 5'-amide (i.e. I; T = thymin-1-yl), a 5'-phosphodiester (i.e. II) or 5'-phosphonate linkages (i.e. III; R = H, thymin-1-ylacetyl) at the junction site are described. The 5'-linkages were installed using protected phosphoramidite and phosphonate building blocks. It is shown that ***PNA*** -(5')-DNA of types I, II, and III (R = thymin-1-ylacetyl) have a higher binding affinity with complementary RNA than native DNA, and that the ***antisense*** activity is mainly due to RNase H.
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 231 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:173994 CAPLUS
DN 128:304468
TI Localization of trinucleotide repeat sequences in myotonic dystrophy cells using a single fluorochrome-labeled ***PNA*** probe
AU Taneja, Krishan L.
CS Univ. Massachusetts Med. Cent., Worcester, MA, USA

SO BioTechniques (1998), 24(3), 472-476 CODEN: BTNQDO; ISSN: 0736-6205
PB Eaton Publishing Co.
DT Journal
LA English
AB A labeled ***peptide*** ***nucleic*** ***acid*** (***PNA***) ***antisense*** probe was used to study the spatial distribution of triplet repeats (CTG) in human myotonic dystrophy (DM) cells by high-resoln. fluorescence in situ hybridization (FISH). It was found that transcripts contg. triplet repeats were present as a no. of discrete foci in the DM nuclei. Greater nos. of foci were visible with the ***PNA*** probe than a comparable DNA probe. The ***PNA*** probe was also used to visualize the triplet-repeat expansion within the DM gene located on chromosome 19. Using the intensity of the expanded triplet-repeat on the chromosomes as a ref., it was estd. there were between 15-230 RNA mols. in each focus obsd. in DM nuclei.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 232 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:145285 CAPLUS
DN 128:253444
TI Contrasting effects of ***PNA*** invasion of the chimeric DMMYC gene on transcription of its myc and PVT domains
AU Boffa, Lidia C.; Carpaneto, Elisabetta M.; Mariani, Maria R.; Louissaint, Marjorie; Allfrey, Vincent G.
CS Department of Experimental Oncology, Istituto per la Ricerca sul Cancro, Genoa, 16132, Italy
SO Oncology Research (1997), 9(1), 41-51 CODEN: ONREE8; ISSN: 0965-0407
PB Cognizant Communication Corp.
DT Journal
LA English
AB A ***peptide*** ***nucleic*** ***acid*** (***PNA***) complementary to a unique DNA sequence in the second exon of the human myc proto-oncogene was tested for its effects on transcription in colonic adenocarcinoma cells in which myc had been amplified and rearranged. A prominent rearrangement in this human cell line (COLO320-DM) involves the insertion of exon 1 of the PVT gene, which is normally located 57 kb downstream, into the first myc intron. We compared the effects of ***PNA*** invasion of the resulting chimeric gene (DMMYC) on sense and ***antisense*** transcription of its myc and PVT domains. Run-on transcription expts. showed that ***PNA*** binding to the unique myc sequence was highly specific and strongly inhibited sense transcription of four unique myc sequences downstream of the ***PNA*** .cntdot.DNA hybridization site, the extent of inhibition at each sequence depending on the duration of exposure to ***PNA*** , and the distance between the downstream myc sequence and the ***PNA*** block. The same ***PNA*** also inhibited ***antisense*** transcription of unique myc sequences upstream of the binding site, confirming that transit of the RNA polymerase II complexes was impaired in both directions. The inhibitory effect of ***PNA*** on upstream ***antisense*** transcription extended beyond the recombination site into the contiguous PVT domain of the chimeric DMMYC gene. In contrast, the same ***PNA*** did not inhibit PVT transcription in a cell line (Raji lymphoma) in which PVT rearrangement did not involve the myc locus.
RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 233 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:141654 CAPLUS
TI ***Peptide*** ***Nucleic*** ***Acid*** (***PNA***) inhibits helicase activity.
AU Tackett, Alan J.; Goodwin, Thomas E.; Morris, Patrick; Raney, Kevin D.
CS Department Chemistry, Hendrix College, Conway, AR, 72032, USA
SO Book of Abstracts, 215th ACS National Meeting, Dallas, March 29-April 2 (1998), CHED-177 Publisher: American Chemical Society, Washington, D. C. CODEN: 65QTAA
DT Conference; Meeting Abstract
LA English
AB ***Peptide*** ***Nucleic*** ***Acid*** (***PNA***) is an analog of DNA in which the deoxyribose phosphate backbone has been replaced by N-(2-aminoethyl) glycine units although the purine and pyrimidine bases are the same as in DNA. ***PNA*** has been suggested as a candidate for ***anti*** - ***sense*** based therapies. We report that ***PNA*** can bind to and inhibit the activity of helicases, enzymes that unwind double-stranded DNA. Binding of ***PNA*** to the bacteriophage T4 Dda helicase was measured using fluorescence titrns. A 13-mer ***PNA*** was found to bind with a dissocn. const. that approached that of the analogous DNA sequence. The ssDNA stimulated ATPase activity of the helicase was inhibited in a competitive manner by the 13-mer ***PNA*** suggesting that the ***PNA*** binds to the helicase in the same binding site as ssDNA. A simple method for prepg. ***PNA*** will also be described.

L9 ANSWER 234 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:81929 CAPLUS
DN 128:167695
TI Design and synthesis of chiral peptidic nucleic acids
AU Ciapetti, Paola; Mann, Andre; Schoenfelder, Angele; Taddei, Maurizio; Trifilieff, Elisabeth; Canet, Isabelle; Canet, Jean Louis
CS Dep. Chimica, Univ. Sassari, Sassari, I-07100, Italy
SO Letters in Peptide Science (1997), 4(4/5/6), 341-349 CODEN: LPSCEM; ISSN: 0929-5666
PB Kluwer Academic Publishers
DT Journal
LA English
AB Due to the increasing interest in the use of oligonucleotide analogs as ***antisense*** and antigene drugs, the authors designed a chiral analog constituted of a peptide frame bearing nucleobases in suitable positions (C- ***PNA***). The authors recently reported the synthesis of four nonnatural .alpha.-amino acids with the DNA bases in the lateral chain. In this paper they present an improved synthesis of the 9-fluorenylmethoxycarbonyl (Fmoc) monomers I-IV and their polymn. to polypeptidic oligonucleotide analogs using a modification of the std. protocol for solid phase peptide synthesis.
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 235 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:38451 CAPLUS
DN 128:128285
TI Preparation of ***peptide*** ***nucleic*** ***acid*** oligomers as ***anti*** - ***sense*** oligonucleotides.
IN Jordan, Stephan; Kosch, Winfried; Kretschmer, Axel; Schwemler, Christoph; Stropp, Udo
PA Bayer A.-G., Germany
SO Ger. Offen., 18 pp. CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------

PI DE 19635064 A1 19980108 DE 1996-19635064 19960830 EP 816379 A2 19980107 EP 1997-109741 19970616 EP 816379 A3 19980401 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI JP 10087634 A2 19980407 JP 1997-181890 19970624
PRAI DE 1996-19625782 19960627 DE 1996-19635064 19960830
OS MARPAT 128:128285
AB Chain- and/or side-chain-modified PNAs [I; A = CO, CHR, CRR', (CH2)n, n = 0-2; R, R' = OH, alkyl, aralkyl, substituted (hetero)aryl; B = (un)natural N-(un)protected base; C = CH, CR; D = NH, NR, CH2, CHR, CRR'; E = NH, NR, CH2, CHR, CRR', O, S, (CH2)n, n = 0-2; F, M independently = CH2, CO, SO2, SO, CS; G = NH, NR, O, S, (CH2)n, n = 3, 4;J = (CH2)2, CR1R2; R1 = H, Me; R2 = H, substituted alkyl, aryl, aralkyl, (CH2)n, n = 3,4; L = (CH2)p, p = 0-2, CHR, CRR'; Q = NH, O, S, NR3; R3 = alkyl, alkenyl, Ph, C5H5N, aralkyl; K = H, support, protecting group, CO of (un)natural amino acid; T = OH, support, protecting group, N of (un)natural amino acid; r = 0,1; s = 1-30] were prepd. as ***anti*** - ***sense*** oligonucleotides for nucleic acid hybridization. Thus, H-(T1-T2)6-Lys-NH2 [T2 = N.alpha.-(thymin-1-ylacetyl)-N.alpha.-(2-aminoethyl)glycyl; T1 = N.delta.-Boc-N.alpha.-Me-N.alpha.-(thymin-1-ylacetyl)-L-ornithinyl] (II) was prepd. using solid-phase synthesis from the component monomers (prep. given). In annealing and gel-shift anal. expts., II was shown to bind with (dA)12. In plasmid-DNA expts., II was shown to inhibit a 4880-base-pair circular plasmid DNA contg. a (dA)12 region.

L9 ANSWER 236 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:30501 CAPLUS
DN 128:115214
TI Synthesis of oligo(5-aminopentanoic acid)-nucleobases (APN): potential ***antisense*** agents
AU Bergmeier, Stephen C.; Fundy, Susan L.
CS Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, The Ohio State University, Columbus, OH, 43210-1291, USA
SO Bioorganic & Medicinal Chemistry Letters (1997), 7(24), 3135-3138 CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Oligomers of 5-aminopentanoic acid nucleobases have been prepd. for use an ***antisense*** agents. The synthesis of the 5'-end starter unit and the 3'-end monomer unit, as well as the coupling procedures used for oligomer formation are described. For example, the trimeric 5-aminopentanoate-based nucleobase I (Cbz = PhCH2OCO; Boc = Me3COCO) was prepd. in 51% yield using the starting materials of NH(CH2CH2OH)2, 2-oxopiperidine and N3-benzoylthymine.
RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 237 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:805585 CAPLUS
DN 128:58277
TI Massively parallel sequencing of sorted polynucleotides using oligonucleotide tags
IN Brenner, Sydney
PA Lynx Therapeutics, Inc., USA
SO U.S., 26 pp., Cont.-in-part of U.S. Ser. No. 322,348, abandoned. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 11 PATENT NO. KIND DATE APPLICATION NO. DATE ---
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PI US 5695934 A 19971209 US 1994-359295 19941219 US 5863722 A 19990126 US 1995-485105 19950607 WO 9612039 A1 19960425 WO 1995-US12678 19951012 W: AU, CA, CZ, FI, HU, JP, KR, NO, SG RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE AU 9539461 A1 19960506 AU 1995-39461 19951012 EP 786014 A1 19970730 EP 1995-937322 19951012 EP 786014 B1 19991215 R: BE, CH, DE, DK, FR, GB, GR, IT, NL, SE EP 952216 A2 19991027 EP 1999-105019 19951012 EP 952216 A3 20000119 R: BE, CH, DE, DK, FR, GB, IT, LI, NL, SE EP 931165 A1 19990728 EP 1996-940238 19961011 R: CH, DE, FR, GB, LI JP 2000511045 T2 20000829 JP 1997-515240 19961011 US 6140489 A 20001031 US 1998-183650 19981030 US 6228589 B1 20010508 US 2000-269911 20000228
PRAI US 1994-322348 B2 19941013 US 1994-359295 A1 19941219 US 1995-485105 A1 19950607 EP 1995-937322 A3 19951012 WO 1995-US12678 W 19951012 WO 1996-US16342 W 19961011
AB The invention provides a method and materials for sorting polynucleotides with oligonucleotide tags. Oligonucleotide tags of the invention are capable of hybridizing to complementary oligomeric compds. consisting of subunits having enhanced binding strength and specificity as compared to natural oligonucleotides. Such complementary oligomeric compds. are referred to herein as tag complements. Subunits of tag complements may consist of monomers of non-natural nucleotide analogs, referred to herein as ***antisense*** monomers or they may comprise oligomers having lengths in the range of 3-6 nucleotides or analogs thereof, including ***antisense*** monomers, the oligomers being selected from a minimally cross-hybridizing set. In such a set, a duplex made up of an oligomer of the set and the complement of any other oligomer of the set contains .gtoreq.2 mismatches. Preferred ***antisense*** monomers include ***peptide*** ***nucleic*** ***acid*** monomers and nucleoside phosphoramidates having a 3'-NHP(O)(O--)O-5' linkage with its adjacent nucleoside. An important aspect of the invention is the use of the oligonucleotide tags for sorting polynucleotides by specifically hybridizing tags attached to the polynucleotides to their complements on solid phase supports. This embodiment provides a readily automated system for manipulating and sorting polynucleotides, particularly useful in large-scale parallel operations, such as large-scale DNA sequencing, mRNA fingerprinting, or the like, wherein many target polynucleotides or many segments of a single target polynucleotide are sequenced simultaneously. Prepn. of an oligonucleotide clamp XO1GO2Y (O1,O2 = oligonucleotides specific for the oligonucleotide tag; G = hinge region such as polyethylene glycol; X,Y = binding moieties such as cholesterol binding moieties) for a specific oligonucleotide tag and parallel sequencing of SV 40 fragments are shown.

L9 ANSWER 238 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:795418 CAPLUS
DN 128:150676
TI ***Peptide*** ***nucleic*** ***acid*** (***PNA***)
From DNA recognition to ***antisense*** and DNA structure
AU Nielsen, Peter E.
CS Blegdamsvej 3c, Department of Medical Biochemistry and Genetics, Center for Biomolecular Recognition, Biochemistry Laboratory B, The Panum Institute, Copenhagen, DK-2200 N, Den.
SO Biophysical Chemistry (1997), 68(1-3), 103-108 CODEN: BICIAZ; ISSN: 0301-4622
PB Elsevier Science B.V.
DT Journal; General Review
LA English
AB A review, with .apprx.32 refs. The biophys. and biol. properties of ***PNA*** (***peptide*** ***nucleic***

acid) is briefly reviewed with special emphasis on recent three dimensional structures of ***PNA*** -nucleic acid complexes and on structure-activity relations in terms of nucleic acid hybridization properties.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 239 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:775524 CAPLUS
DN 128:110389
TI Spermine conjugated peptide nucleic acids (spPNA): UV and fluorescence studies of ***PNA*** -DNA hybrids with improved stability
AU Gangamani, Bargur P.; Kumar, Vaijayanti A.; Ganesh, Krishna N.
CS Organic Chemistry Synthesis Division, National Chemical Laboratory, Pune, 411008, India
SO Biochemical and Biophysical Research Communications (1997), 240(3), 778-782 CODEN: BBRCA9; ISSN: 0006-291X
PB Academic Press
DT Journal
LA English
AB Peptide Nucleic Acids (PNAs), the achiral DNA mimics with amide backbone, are emerging as attractive leads for drug development by ***antisense*** approach. Two major limitations of PNAs from an application perspective are their limited soly. in aq. systems and pronounced self-organization. In this paper, it is shown that covalent conjugation of spermine at C-terminus of ***PNA*** (spPNA) improves its soly. and binds to complementary DNA 20 times stronger than the corresponding binding of ***PNA*** . Fluorescence kinetics shows a 2 fold acceleration of the bimol. assocn. process in spPNA:DNA hybrids, due to electrostatic interaction cationic spermine tagged to ***PNA*** with anionic DNA. This modification is easy to incorporate into ***PNA*** synthetic protocols to make them more effective in biol. applications and may improve the poor cell uptake of ***PNA*** .
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 240 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:740255 CAPLUS
DN 128:31076
TI Gene therapy for mitochondrial DNA defects using peptide nucleic acids, especially ***PNA*** -mitochondrial targeting peptide conjugates
IN Turnbull, Douglas Matthew; Lightowlers, Robert Neil; Taylor, Robert William
PA University of Newcastle Upon Tyne, UK; Turnbull, Douglas Matthew; Lightowlers, Robert Neil; Taylor, Robert William
SO PCT Int. Appl., 39 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9741150 A2 19971106 WO 1997-GB1102 19970422 W: JP, US RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRAI GB 1996-8803 19960427
AB The invention concerns a method for selectively preventing the replication of mitochondrial DNA using complementary PNAs; and the PNAs for use in the method. The PNAs may be targeted to the mitochondria by conjugating the PNAs with a mitochondrial targeting peptide. PNAs targeted to mitochondrial point and deletion mutations sequence-specifically inhibited expression of the genes in vitro. A ***PNA*** -cytochrome c oxidase subunit VIII N-terminal peptide conjugate was shown to localized to mitochondria in myotubes.

L9 ANSWER 241 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:684528 CAPLUS
DN 127:355966
TI Cloning and sequencing of hereditary hemochromatosis gene with therapeutic and diagnostic approaches for disease treatment
IN Thomas, Winston J.; Drayna, Dennis T.; Feder, John N.; Gnirke, Andreas; Ruddy, David; Tsuchihashi, Zenta; Wolff, Roger K.
PA Mercator Genetics, Inc., USA; Thomas, Winston J.; Drayna, Dennis T.; Feder, John N.; Gnirke, Andreas; Ruddy, David; Tsuchihashi, Zenta; Wolff, Roger K.
SO PCT Int. Appl., 114 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9738137 A1 19971016 WO 1997-US6254 19970404 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG US 5712098 A 19980127 US 1996-632673 19960416 US 6025130 A 20000215 US 1996-652265 19960523 AU 9726701 A1 19971029 AU 1997-26701 19970404 AU 733459 B2 20010517 EP 954602 A1 19991110 EP 1997-918642 19970404 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI US 1996-630912 A2 19960404 US 1996-632673 A2 19960416 US 1996-652265 A2 19960523 WO 1997-US6254 W 19970404
AB The identification, isolation, and cloning of the DNA sequence, transcripts and gene products corresponding to the gene and mutations that are responsible for the disease hereditary hemochromatosis (HH) is presented. Methods are presented for PCR screening for HH homozygotes and further relates to HH diagnosis, prenatal screening and diagnosis, and therapies of HH disease, including gene therapeutics, protein and antibody based therapeutics, and small mol. therapeutics.

L9 ANSWER 242 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:684422 CAPLUS
DN 128:1459
TI Inhibitor peptide nucleic acids binding the RNA component of mammalian telomerase
IN Shay, Jerry W.; Wright, Woodring E.; Piatyszek, Mieczyslaw A.; Corey, David; Norton, James C.
PA Geron Corp., USA
SO PCT Int. Appl., 75 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9738013 A1 19971016 WO 1997-US5931 19970409 W: AU, CA, CN, JP, KR, MX RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE US 6015710 A 20000118 US 1996-630019 19960409 AU 9726631 A1 19971029 AU 1997-26631 19970409 JP 2001517929 T2 20011009 JP 1997-536487 19970409
PRAI US 1996-630019 A 19960409 WO 1997-US5931 W 19970409

AB Peptide nucleic acids (PNAs) that can bind with the RNA moiety of mammalian telomerases and that can inhibit the enzyme are described. The PNAs may be ***antisense*** or triple helix- or D-loop-forming. The PNAs may be further modified with lipid moieties or signal peptides to ensure their efficient uptake by animal cells. The PNAs can be used to assay telomerase activity and to inhibit the enzyme in the treatment of disease. A series of ***PNA*** candidates for inhibition of telomerase activity were tested for efficacy in a telomere repeat amplification protocol assay and inhibition in the micromolar or nanomolar range was found. Further optimization expts. are reported.

L9 ANSWER 243 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:618108 CAPLUS
DN 127:273861
TI Substituted nucleic acid mimics for use in hybridization and regulation of gene expression
IN Nielsen, Peter E.; Christensen, Leif; Hansen, Henrik Frydenlund
PA Isis Pharmaceuticals, Inc., USA; Nielsen, Peter E.; Christensen, Leif; Hansen, Henrik Frydenlund
SO PCT Int. Appl., 40 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9732888 A1 19970912 WO 1997-US3584 19970307 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG AU 9720723 A1 19970922 AU 1997-20723 19970307 EP 885238 A1 19981223 EP 1997-908939 19970307 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI JP 11507950 T2 19990713 JP 1997-531960 19970307 JP 3452584 B2 20030929
PRAI US 1996-612661 A2 19960308 WO 1997-US3584 W 19970307
OS MARPAT 127:273861
AB Compns. and methods are provided for the nucleic acid mimic detn. of nucleic acids. The compns. and methods may be used in the diagnosis and treatment of diseases amenable through modulation of nucleic acids which encode proteins that are implicated in disease states. In accordance with preferred embodiments, mimics are comprised of non-naturally occurring backbones to which are appended modified heterocyclics bases. Such bases preferably have sterically balky substituents 1, 2, or 3 atoms removed from the sites of attachment to the backbone. Homopyrimidine peptide nucleic acids contg. N-4-benzoylcytosine were prepd. When these PNAs were incubated with target nucleic acid at pH 7, the benzoyl group interfered with triplex formation but not duplex formation.

L9 ANSWER 244 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:612554 CAPLUS
DN 127:302738
TI Progress in developing ***PNA*** as a gene-targeted drug
AU Good, Liam; Nielsen, Peter E.
CS Center for Biomolecular Recognition, Department of Medical Biochemistry and Genetics, University of Copenhagen, Panum Institute, Copenhagen, Den.
SO Antisense & Nucleic Acid Drug Development (1997), 7(4), 431-437 CODEN: ANADF5; ISSN: 1087-2906
PB Liebert
DT Journal; General Review
LA English
AB A review with 55 refs. ***Peptide*** ***nucleic*** ***acid*** (***PNA***) is a DNA mimic in which the nucleobases are attached to a pseudopeptide backbone. This achiral, uncharged, and rather flexible peptide backbone permits more stable hybridization to DNA and RNA oligomers with uncompromised or even improved sequence selectivity. Addnl. advantages of ***PNA*** are stability against nucleases and proteases and convenient solid phase synthesis. At the RNA level, ***PNA*** can be targeted to mRNA to block protein synthesis in an ***antisense*** strategy. ***PNA*** can also be targeted to the RNA component of ribonucleoproteins (RNPs) to inhibit their enzymic activities. At the DNA level, the unique ability of ***PNA*** to bind DNA by duplex invasion can be used to arrest transcription within a gene sequence or to provide an artificial open complex to promote transcription. This review focuses on recent progress toward the development of ***PNA*** as a sequence-targeted drug.
RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 245 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:524164 CAPLUS
DN 127:171910
TI ***Peptide*** ***nucleic*** ***acid***
AU Oerum, Henrik; Kessler, Christoph; Koch, Troels
CS PNA Diagnostics A/S, Copenhagen, Den.
SO Nucleic Acid Amplification Technologies (1997), 29-43. Editor(s): Lee, Helen H.; Morse, Stephen A.; Olsvik, Oerjan. Publisher: Eaton, Natick, Mass. CODEN: 64URAH
DT Conference; General Review
LA English
AB A review with >75 refs. on ***peptide*** ***nucleic*** ***acid*** chem., and its use as a tool in mol. biol., nucleic acid diagnostics and ***antisense*** therapeutics.

L9 ANSWER 246 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:506491 CAPLUS
DN 127:229232
TI Transformed and immortalized cellular uptake of oligodeoxynucleoside phosphorothioates, 3'-alkylamino oligodeoxynucleotides, 2'-O-methyl oligoribonucleotides, oligodeoxynucleoside methylphosphonates, and peptide nucleic acids
AU Gray, Gary D.; Basu, Soumitra; Wickstrom, Eric
CS Dep. of Microbiol. and Immunol. and Kimmel Cancer Cent., Thomas Jefferson Univ., Philadelphia, PA, 19107, USA
SO Biochemical Pharmacology (1997), 53(10), 1465-1476 CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier
DT Journal
LA English
AB Direct quant. comparisons of cellular uptake across a wide variety of analogs and cell types are necessary for the design of oligonucleotide diagnostic and therapeutic applications. This work reports quant. cellular uptake and nuclear localization of [14C]oligodeoxynucleoside phosphorothioates (PS), 3'-alkylamino oligodeoxynucleoside phosphodiesters (PO-NH2), 2'-O-Me oligoribonucleoside phosphodiesters (2OM), peptide nucleic acids (***PNA***), and oligodeoxynucleoside methylphosphonates (MP) in several transformed or immortalized cell lines. All analogs demonstrated active cellular uptake in that intracellular concns. greatly exceeded the extracellular 1 .mu.M concn. within 1-3 h. However, by 9-24 h, cellular accumulations of PS exceeded those of PO-NH2 and 2OM by 3- to 5-fold, ***PNA*** by 6- to 7-fold,

and MP by 8- to 10-fold. Similar results were obsd. in two transformed cell lines, HL-60 leukocytes and H-ras transformed fibroblasts, using three different heterogeneous sequences. H-ras and IGF-1R transformed fibroblasts had a 2- to 5-fold higher uptake of all analogs than non-transformed immortalized fibroblasts. Nuclear levels of the PO-NH2, PS, and MP analogs were approx. 25% of total cellular uptake, while nuclear percentages of 2OM and ***PNA*** were less than 20%, suggesting some differences in nuclear localization among the analogs. These observations provide a direct quant. comparison of cellular uptake as a function of oligonucleotide modification, and imply that transformation enhances cellular uptake. From the perspective of therapy and diagnosis, clear trade-offs were apparent between efficiency of uptake on the one hand, and nuclease resistance and hybridization strength on the other.

L9 ANSWER 247 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:481418 CAPLUS
DN 127:218223
TI Synthesis, uptake, and intracellular metabolism of a hydrophobic tetrapeptide- ***peptide*** ***nucleic*** ***acid*** (***PNA***)-biotin molecule
AU Scarfi, Sonia; Gasparini, Anna; Damonte, Gianluca; Benatti, Umberto
CS Institute of Biochemistry, University of Genoa, Genoa, 16132, Italy
SO Biochemical and Biophysical Research Communications (1997), 236(2), 323-326 CODEN: BBRCA9; ISSN: 0006-291X
PB Academic
DT Journal
LA English
AB ***Peptide*** ***nucleic*** ***acid*** (***PNA***) mols. are very promising tools for antigene and ***antisense*** therapies because of their remarkable refractoriness to degrdn. in biol. fluids. However, very limited information is available on their uptake by potentially target cells and on their intracellular fate. A membrane-diffusable and fluorescence detectable ***PNA*** chimera, Phe-Leu-Phe-Leu-(adenine)3-biotin, was obtained by solid phase peptide synthesis and characterized by combined HPLC and mass spectrometry (MS). This ***PNA*** chimera was found to permeate across the membrane of both human erythrocytes and B Namalwa cells much more extensively and rapidly than a control Gly-(Adenine)3-biotin ***PNA*** mol. Fluorescence patterns of internalization were consistent for a diffusion process resulting in the appearance of uniform cytoplasmic distribution of the hydrophobic peptide- ***PNA*** chimera in the Namalwa cells. Degrdn. of the synthesized ***PNA*** chimera by cell lysates and to a much slower extent by the intact Namalwa cells was investigated by HPLC-MS analyses of the corresponding methanol exts. It involved the progressive removal of each of the hydrophobic amino acid residues, while the linkage with the biotin label was completely resistant to cleavage. These results hold promise for the design and synthesis of membrane-permeable ***PNA*** sequences suitable for antigene therapies.

L9 ANSWER 248 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:433595 CAPLUS
DN 127:95571
TI Synthesis and Characterization of a ***Peptide*** ***Nucleic*** ***Acid*** Conjugated to a D-Peptide Analog of Insulin-like Growth Factor 1 for Increased Cellular Uptake
AU Basu, Soumitra; Wickstrom, Eric
CS Department of Microbiology and Immunology and Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA, 19107, USA
SO Bioconjugate Chemistry (1997), 8(4), 481-488 CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
AB DNA therapeutics show great potential for gene-specific, nontoxic therapy of a wide variety of diseases. The deoxyribose phosphate backbone of DNA has been modified in a no. of ways to improve nuclease stability and cell membrane permeability. Recently, a new DNA deriv. with an amide backbone instead of a deoxyribose phosphate backbone, ***peptide*** ***nucleic*** ***acid*** (***PNA***), has shown tremendous potential as an ***antisense*** agent. Although PNAs hybridize very strongly and specifically to RNA and DNA, they are taken up by cells very poorly, limiting their potential as nucleic acid binding agents. To improve cellular uptake of a ***PNA*** sequence, it was conjugated to a D-amino acid analog of insulin-like growth factor 1 (IGF1), which binds selectively to the cell surface receptor for insulin-like growth factor 1 (IGF1R). The IGF1 D-peptide analog was assembled on (4- methylbenzhydryl)amine resin, and then the ***PNA*** was extended as a continuation of the peptide. The conjugate and control sequences were radiolabeled with 14C or fluorescently labeled with fluorescein isothiocyanate. Cellular uptake of the ***PNA*** -peptide conjugate, a control with two alanines in the peptide, and a control ***PNA*** without the peptide segment were studied in murine BALB/c 3T3 cells, which express low levels of murine IGF1R, in p6 cells, which are BALB/c 3T3 cells which overexpress a transfected human IGF1R gene, and in human Jurkat cells, which do not express IGF1R, as a neg. control. The specific ***PNA*** -peptide conjugate displayed much higher uptake than the control ***PNA*** , but only in cells expressing IGF1R. This approach may allow cell-specific and tissue-specific application of PNAs as gene-regulating agents in vivo.

L9 ANSWER 249 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:381831 CAPLUS
DN 127:104863
TI Efficient in vitro inhibition of HIV-1 gag reverse transcription by ***peptide*** ***nucleic*** ***acid*** (***PNA***) at minimal ratios of ***PNA*** /RNA
AU Koppelhus, Uffe; Zachar, Valadimir; Nielsen, Peter E.; Liu, Xiangdon; Eugen-Olsen, Jesper; Ebbesen, Peter
CS Dep. Virus and Cancer, Danish Cancer Society, Aarhus, DK-8000, Den.
SO Nucleic Acids Research (1997), 25(11), 2167-2173 CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB The authors have tested the inhibitory potential of ***peptide*** ***nucleic*** ***acid*** (***PNA***) on in vitro reverse transcription of the HIV-1 gag gene. ***PNA*** was designed to target different regions of the HIV-1 gag gene and the effect on reverse transcription by HIV-1, MMLV and AMV reverse transcriptases (RTs) was investigated. The authors found that a bis- ***PNA*** (parallel ***antisense*** 10mer linked to antiparallel ***antisense*** 10mer) was superior to both the parallel ***antisense*** 10mer and antiparallel ***antisense*** 10mer in inhibiting reverse transcription of the gene, thus indicating triplex formation at the target sequence. A complete arrest of reverse transcription was obtained at .apprx.6-fold molar excess of the bis- ***PNA*** with respect to the gag RNA. At this molar ratio the authors found no effect on in vitro translation of gag RNA. A 15mer duplex-forming ***PNA*** was also found to inhibit reverse transcription at very low molar ratios of ***PNA*** /gag RNA. Specificity of the inhibition of reverse

transcription by ***PNA*** was confirmed by RNA sequencing, which revealed that all tested RTs were stopped by the ***PNA*** /RNA complex at the predicted site. The authors propose that the effect of ***PNA*** is exclusively due to steric hindrance, as we found no signs of RNA degrdn. that would indicate ***PNA*** -mediated RNase H activation of the tested RTs. In conclusion, ***PNA*** appears to have a potential to become a specific and efficient inhibitor of reverse transcription in vivo, provided sufficient intracellular levels are achievable.
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 250 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:219832 CAPLUS
DN 126:305772
TI New hetero-oligomeric peptide nucleic acids with improved binding properties to complementary DNA
AU Jordan, Stephan; Schwemler, Christoph; Kosch, Winfried; Kretschmer, Axel; Stropp, Udo; Schwenner, Eckhardt; Mielke, Burkhard
CS Bayer AG, Central Research, Leverkusen, D-51368, Germany
SO Bioorganic & Medicinal Chemistry Letters (1997), 7(6), 687-690 CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier
DT Journal
LA English
AB Hetero-oligomeric PNAs consisting of new monomeric building blocks L-trans-I, L-cis-I, D-trans-I, II, and III (X = O) and various amts. of N-(2-aminoethyl)glycine (IV) have been synthesized by solid-phase chem. Some of these new compds. show stronger binding to complementary DNA than the original PNAs, and are consequently very interesting candidates as ***antisense*** compds. for applications in therapy and in diagnostics.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 251 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:188948 CAPLUS
DN 126:293593
TI Nucleic acid analog peptide (NAAP).2. Syntheses and properties of novel DNA analog peptides containing nucleobase linked .beta.-amino alanine
AU Fujii, Masayuki; Yoshida, Kohya; Hidaka, Jinsai
CS Department of Industrial Chemistry, Faculty of Engineering in Kyushu, Kinki University, Fukuoka, 820, Japan
SO Bioorganic & Medicinal Chemistry Letters (1997), 7(5), 637-640 CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier
DT Journal
LA English
AB As substitutes for ***antisense*** and triplex oligonucleotides, oligopeptides contg. N.beta.-(thymin-1-ylacetyl)-.beta.-aminoalanine and N.beta.-(cytosin-1-ylacetyl)-.beta.-aminoalanine moieties were synthesized on solid support using std. Boc-chem and protected building blocks I and II. The obtained peptide contg. ten thymine bases was shown to form a hybrid duplex with a complementary oligo DNA, dA10, with a melting temp. (Tm) of 36.5.degree. at pH 7.0.
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 252 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:160790 CAPLUS
TI Structures of reptide-nucleic acids (***PNA***) bound to RNA, DNA, and ***PNA***
AU Brown, Stephen C.; Thomson, Steven A.; Josey, John A.; Fred Hassman, C.; Veal, James; Davis, Donald G.
CS Glaxo Wellcome Research and Development, Research Triangle Park, NC, 27709, USA
SO Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17 (1997), COMP-162 Publisher: American Chemical Society, Washington, D. C. CODEN: 64AOAA
DT Conference; Meeting Abstract
LA English
AB Peptide Nucleic Acids (PNAs) contain the std. bases found in nucleic acids, while the phosphoribose backbone is replaced by a peptide-like moiety amenable to polymn. via automated solid-phase synthesis using std. peptide chemistries. PNAs of various sequences demonstrate high affinity and mismatch sensitivity to sequence-complementary nucleic acid strands. Such properties represent a significant advance in the design of ***antisense*** and antigene agents. Structures of ***PNA*** -RNA, ***PNA*** -DNA, and ***PNA*** - ***PNA*** duplexes and/or triplexes have been detd. using NMR methods. These structures demonstrate std. Watson-Crick and Hoogsteen base-pairing schemes comparable to more familiar double & triple-stranded nucleic acid structures, with the ***PNA*** backbone adapting as required.

L9 ANSWER 253 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:139016 CAPLUS
DN 126:238623
TI Chemistry, properties and applications of ***PNA*** (***peptide*** ***nucleic*** ***acid***)
AU Dueholm, Kim L.; Nielsen, Peter E.
CS Cent. Biomol. Recognition, Panum Inst., Copenhagen, DK-2200, Den.
SO New Journal of Chemistry (1997), 21(1), 19-31 CODEN: NJCHE5; ISSN: 1144-0546
PB Gauthier-Villars
DT Journal; General Review
LA English
AB A review with 98 refs. ***Peptide*** ***Nucleic*** ***Acid*** (***PNA***) is conceptually a DNA analog, but in a chem. sense ***PNA*** bridges peptides and nucleic acids by virtue of its pseudopeptide backbone and its nucleobases. Since this mimic was introduced five years ago, convenient synthetic routes to ***PNA*** monomers as well as oligomers have been devised, and a no. of structural modifications have been introduced into ***PNA*** . In addn., extensive research has shed light on the interesting properties of ***PNA*** , demonstrating the development potential of ***PNA*** into biomol. tools, as well as ***antisense*** and/or antigene drugs. This review focuses primarily on the chem. aspects of ***PNA*** and its modifications, including the introduction of chirality, the elongation of the pseudopeptide backbone as well as the permutation of functional groups within the backbone, and the introduction of a non-natural nucleobase. In addn., the effects of covalently linking two ***PNA*** oligomers will be described. Furthermore, the ability of ***PNA*** to hybridize to DNA or RNA targets with a high sequence specificity will be discussed, as will the secondary structure of such hybrids and that of ***PNA*** itself. Finally, (potential) applications of ***PNA*** are briefly dealt with herein.

L9 ANSWER 254 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:62872 CAPLUS
DN 126:128306
TI ***Peptide*** ***nucleic*** ***acid***
AU Zheng, Ligang; Min, Jimei; Zhang, Lihe
CS Natl. Key Lab. Natural Biometic Drugs, Beijing Med. Univ., Beijing, 100083, Peop. Rep. China
SO Shengwu Huaxue Yu Shengwu Wuli Jinzhan (1996), 23(3), 209-213 CODEN: SHYCD4; ISSN: 1000-3282

PB Kexue
DT Journal; General Review
LA Chinese
AB A review, with 22 refs., on ***peptide*** ***nucleic*** ***acid*** (***PNA***) with subdivision headings (1) structure and function relation; (2) synthesis; (3) hybridization characteristics; (4) bio-mol. research; (5) ***antisense*** activity and (6) conclusion.

L9 ANSWER 255 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:13375 CAPLUS
DN 126:114098
TI Specific and nonspecific inhibition of transcription by DNA, ***PNA*** , and phosphorothioate promoter analog duplexes
AU Hamilton, Susan E.; Iyer, Mridula; Norton, James C.; Corey, David R.
CS Southwest. Med. Cent., Univ. Texas, Dallas, TX, 75235, USA
SO Bioorganic & Medicinal Chemistry Letters (1996), 6(23), 2897-2900 CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier
DT Journal
LA English
AB DNA duplexes analogous to the promoters for SP6 or T7 RNA polymerase inhibit transcription with exquisite selectivity. By contrast, phosphorothioate oligomers inhibit nonselectively, and ***peptide*** ***nucleic*** ***acid*** (***PNA***) duplexes and ***PNA*** :DNA heteroduplexes do not inhibit at all. The absence of recognition of proteins by PNAs may prove to be a substantial advantage for their use as ***antisense*** agents and nucleic acid probes.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 256 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:694365 CAPLUS
DN 125:319857
TI Biotinylated EGF coupled with polylysine binds therapeutic genes for delivery into cell and lung cancer gene therapy using tumor suppressor gene targeting
IN Cristiano, Richard J.; Roth, Jack A.
PA University of Texas System, USA
SO PCT Int. Appl., 66 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9630536 A1 19961003 WO 1996-US4017 19960325 W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML AU 9653706 A1 19961016 AU 1996-53706 19960325
PRAI US 1995-410526 19950324 WO 1996-US4017 19960325
AB A receptor-mediated complex that selectivity delivers nucleic acid into cells is disclosed. Epidermal growth factor (EGF)-receptor-binding peptide acts as a targeting ligand and is complexed with a component that binds nucleic acid. A reporter gene conjugated to EGF ***peptide*** / ***nucleic*** ***acid*** -binding agent was successfully transferred into a no. of different cell lines that express high levels of receptor. This is esp. useful for targeting tumor suppressor genes or other therapeutic genes in lung cancer treatment.

L9 ANSWER 257 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:622320 CAPLUS
DN 125:295645
TI Characterization of peptide-oligonucleotide heteroconjugates by mass spectrometry
AU Jensen, Ole N.; Kulkarni, Sandhya; Aldrich, Jane V.; Barofsky, Douglas F.
CS Dep. Biochem. Biophysics, Oregon State Univ., Corvallis, OR, 97331-7301, USA
SO Nucleic Acids Research (1996), 24(19), 3866-3872 CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB Two peptide-oligothymidylic acids, prepd. by joining an 11 residues synthetic peptide contg. one internal carboxyl group (Asp side chain) to amino-linker-5'-pdT6 and amino-linker-5'-pdT10 oligonucleotides, were analyzed by matrix-assisted laser desorption/ionization (MALDI) on a linear time-of-flight mass spectrometer and by electrospray ionization (ESI) on a triple-quadrupole system. These synthetic compds. model ***peptide*** - ***nucleic*** ***acid*** heteroconjugates encountered in ***antisense*** research and in studies that use photochem. crosslinking to investigate mol. aspects of protein-nucleic acid interactions. MALDI and ESI sensitivities for the hybrid compds. were found to be similar resp. to their sensitivities for the pure oligonucleotide parts. In general, MALDI proved to be less affected by sample impurities and more sensitive than ESI, while ESI on the quadrupole produced greater mass accuracy and resoln. than MALDI on the time-of-flight instrument. A hybrid's behavior in a MALDI-matrix or an ESI-spray-solvent was found to be governed mainly by the oligonucleotide. A single pos. ESI tandem mass spectrum of the peptide-dT6 accounted for the heteroconjugate's entire primary structure including the point of the oligonucleotide's covalent attachment to the peptide.

L9 ANSWER 258 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:483575 CAPLUS
DN 125:136916
TI ***Peptide*** ***Nucleic*** ***Acid*** Characterization by MALDI-TOF Mass Spectrometry
AU Butler, John M.; Jiang-Baucom, Ping; Huang, Meng; Belgrader, Phillip; Girard, James
CS Biotechnology Division, National Institute of Standards and Technology, Gaithersburg, MD, 20899, USA
SO Analytical Chemistry (1996), 68(18), 3283-3287 CODEN: ANCHAM; ISSN: 0003-2700
PB American Chemical Society
DT Journal
LA English
AB Peptide nucleic acids (PNAs) are a new class of DNA mimics in which the regular nucleobases of adenine, thymine, cytosine, and guanine are connected via a peptide-like backbone. ***PNA*** mols. retain the same Watson-Crick base pairing as regular oligonucleotides, with the added benefits of greater specificity and resistance to enzymic digestion. While the use of PNAs has grown rapidly because of their potential applications in biotechnol., little work has been done on developing anal. procedures for characterizing them. We have found matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry to be an effective tool for ***PNA*** anal. ***PNA*** mols. survive the MALDI process intact and are easily ionized with almost no multiply-charged species. These features allow mixts. to be easily characterized. Traditional protein matrixes (e.g., sinapinic acid, 2,5-dihydroxybenzoic acid, .alpha.-cyano-4-hydroxycinnamic acid) were found to be superior to DNA matrixes (e.g., trihydroxy-acetophenone, 3-hydroxypicolinic acid, picolinic acid). In addn., the new DNA matrix 6-aza-2-thiothymine

worked well. The ability of MALDI-TOF-MS to ascertain ***PNA*** purity and sequence information at low picomole levels will be important as greater quality control of ***PNA*** synthesis is needed (e.g., when PNAs are used as ***antisense*** or antigene drugs).

L9 ANSWER 259 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:415176 CAPLUS
TI Amino acid nucleic acids: Synthesis and hybridization properties of a novel class of ***antisense*** oligonucleotides.
AU Ramasamy, Kanda S.; Seifert, Wilfried
CS ICN Pharmaceuticals, Inc., Costa Mesa, CA, 92626, USA
SO Book of Abstracts, 212th ACS National Meeting, Orlando, FL, August 25-29 (1996), ORGN-270 Publisher: American Chemical Society, Washington, D. C. CODEN: 63BFAF
DT Conference; Meeting Abstract
LA English
AB Oligonucleotides that specifically recognize mRNA present unique opportunities for the treatment of viral diseases, cancer, and for the study of genetic disorders. In order to be pharmacol. useful, the oligonucleotides must have (a) sufficient binding to its target sequence; (b) sufficient specificity; (c) stability towards exo- and endo-nucleases; (d) penetrate through cell membrane. To meet these criteria derivs. such as phosphorothiates, phosphoramidates, methylphosphonates, formacetal, carbamate, siloxane, sulfur linked, amides, amine, methylhyrroxylamine and ***PNA*** have been examd. However, most of these modifications suffer from one or more forms of criteria. Therefore, the quest to develop new and novel modified oligonucleotides, based on sequence specific interactions between complementary nucleic acid, has sparked recently. Here we will present the synthesis and biophys. properties of Amino Acid Nucleic Acids.

L9 ANSWER 260 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:391733 CAPLUS
DN 125:50733
TI Massively parallel sequencing of sorted polynucleotides using oligonucleotide tags
IN Brenner, Sydney
PA Lynx Therapeutics, Inc., USA
SO PCT Int. Appl., 70 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 11 PATENT NO. KIND DATE APPLICATION NO. DATE ---
---------- ---- -------- ---------- --------
PI WO 9612039 A1 19960425 WO 1995-US12678 19951012 W: AU, CA, CZ, FI, HU, JP, KR, NO, SG RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE US 5695934 A 19971209 US 1994-359295 19941219 AU 9539461 A1 19960506 AU 1995-39461 19951012 EP 786014 A1 19970730 EP 1995-937322 19951012 EP 786014 B1 19991215 R: BE, CH, DE, DK, FR, GB, GR, IT, NL, SE EP 931165 A1 19990728 EP 1996-940238 19961011 R: CH, DE, FR, GB, LI JP 2000511045 T2 20000829 JP 1997-515240 19961011 US 6228589 B1 20010508 US 2000-269911 20000228
PRAI US 1994-322348 A 19941013 US 1994-359295 A 19941219 WO 1995-US12678 W 19951012 WO 1996-US16342 W 19961011
AB The invention provides a method and materials for sorting polynucleotides with oligonucleotide tags. Oligonucleotide tags of the invention are capable of hybridizing to complementary oligomeric compds. consisting of subunits having enhanced binding strength and specificity as compared to natural oligonucleotides. Such complementary oligomeric compds. are referred to herein as "tag complements". Subunits of tag complements may consist of monomers of non-natural nucleotide analogs, referred to herein as " ***antisense*** monomers" or they may comprise oligomers having lengths in the range of 3 to 6 nucleotides or analogs thereof, including ***antisense*** monomers, the oligomers being selected from a minimally cross-hybridizing set. In such a set, a duplex made up of an oligomer of the set and the complement of any other oligomer of the set contains at least two mismatches. Preferred ***antisense*** monomers include ***peptide*** ***nucleic*** ***acid*** monomers and nucleoside phosphoramidates having a 3'-NHP(O)(O-)O-5' linkage with its adjacent nucleoside. An important aspect of the invention is the use of the oligonucleotide tags for sorting polynucleotides by specifically hybridizing tags attached to the polynucleotides to their complements on solid phase supports. This embodiment provides a readily automated system for manipulating and sorting polynucleotides, particularly useful in large-scale parallel operations, such as large-scale DNA sequencing, mRNA fingerprinting, or the like, wherein many target polynucleotides or many segments of a single target polynucleotide are sequenced simultaneously. Prepn. of a oligonucleotide clamp XO1GO2Y (O1,O2=oligonucleotides specific for the oligonucleotide tag; G=hinge such as polyethylene glycol; X,Y=binding moieties such as cholesterol binding moieties) for a specific oligonucleotide tag and parallel sequencing of SV40 fragments were shown.

L9 ANSWER 261 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:335131 CAPLUS
DN 125:50564
TI Invasion of the CAG triplet repeats by a complementary ***peptide*** ***nucleic*** ***acid*** inhibits transcription of the androgen receptor and TATA-binding protein genes and correlates with refolding of an active nucleosome containing a unique AR gene sequence
AU Boffa, Lidia C.; Morris, Patricia L.; Carpaneto, Elisabetta M.; Louissaint, Marjorie; Allfrey, Vincent G.
CS Dep. Experimental Oncol., Inst. Nazionale la Ricerca, Genoa, 16132, Italy
SO Journal of Biological Chemistry (1996), 271(22), 13228-13233 CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB The DNA sequence of the genes for the androgen receptor (AR) and TATA-binding protein (TBP), like many other genes encoding transcription factors, contains a series of tandem CAG repeats. Here we explore the capacity of complementary peptide nucleic acids (PNAs) to invade the CAG triplets of the AR and TBP genes in human prostatic cancer cells and show that the PNAs readily entered the nuclei of lysolecithin-permeabilized cells and effectively inhibited sense transcription of unique AR and TBP DNA sequences downstream of the site of ***PNA*** .cntdot.DNA hybridization, but not upstream of that site. These PNAs had little or no effect on transcription of the c-myc gene, which lacks a CAG triplet domain. Conversely, a ***PNA*** complementary to a unique sequence of the c-myc gene did not inhibit transcription of the AR or TBP genes but did inhibit c-myc transcription. Comparisons of ***PNA*** effects on sense and ***antisense*** transcription of the AR, TBP, and c-myc genes confirm that progression of the RNA polymerase complex beyond the site of ***PNA*** .cntdot.DNA hybridization is impaired in both directions. Suppression of the AR gene results in refolding of a transcriptionally active nucleosome contg. a unique 17-mer AR DNA sequence.

L9 ANSWER 262 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:323535 CAPLUS
DN 125:1419

TI Peptide-based nucleic acid mimics
IN Shah, Vibhakar J.; Kenyon, George L.
PA Regents of the University of California, USA
SO PCT Int. Appl., 130 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9604000 A1 19960215 WO 1995-US9828 19950803 W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG US 5705333 A 19980106 US 1994-286875 19940805 AU 9532750 A1 19960304 AU 1995-32750 19950803
PRAI US 1994-286875 19940805 WO 1995-US9828 19950803
OS CASREACT 125:1419
AB Novel nucleic acid mimics (termed "PENAMs") comprise a peptidic backbone and nucleotidic sidechains; the sidechains are oriented in such a way that the PENAM is homomorphous to target nucleic acids with which it can effectively H bond. Homomorphism is achieved by the incorporation of unusual stereochem. centers, including D chiral centers and quasichiral centers, into the peptidic backbone. The PENAMs are useful for targeting nucleic acid sequences to modulate their activity in an " ***antisense*** " manner. Targeting can also be used to detect, isolate, or modify target nucleic acids. The PENAMs are prepd. from monomers - N(W)S1E(Y)(S3B)S2C(:X)- (E = C, N; W = H, spacer group; Y = H or spacer group if E = C, or electron pair if E = N; S1-S3 = bond, spacer group; X = O, S; B = nucleic acid base or analog), e.g. in an automated peptide synthesizer. H bonding is facilitated by the absence of electrostatic charge repulsion due to replacement of the normally charged backbone. The PENAMs are resistant to degradative enzymes, owing to the absence of phosphodiester bonds and the presence of unusual chiral centers in the backbone. Thus, a PENAM monomer was produced in several steps from homoserine lactone and adenine, and was subjected to solid-phase peptide synthesis to produce PENAM I. I bound to (dT)10 more strongly than did (dA)10.

L9 ANSWER 263 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:135244 CAPLUS
DN 124:253922
TI The affinity of an oligodeoxynucleotide-peptide conjugate for an RNA hairpin loop depends on stereochemistry at the DNA-peptide junction
AU Sahasrabudhe, Parag V.; Gmeiner, William H.
CS Eppley Cancer Inst., Dep. Pharmaceutical Sci., Univ. Nebraska Med. Center, Omaha, NE, 68198-6805, USA
SO Journal of Biomolecular Structure & Dynamics (1996), 13(4), 585-91 CODEN: JBSDD6; ISSN: 0739-1102
PB Adenine Press
DT Journal
LA English
AB Mol. models of an oligodeoxynucleotide-peptide conjugate complexed to an RNA hairpin loop were constructed to assess the effect of stereoisomerism at the point of attachment of the peptide to the oligodeoxynucleotide on the affinity of the conjugate for an RNA target. The peptide portion of the oligodeoxynucleotide-peptide conjugate, (L-lysine)8, was covalently attached to the N-allyl group of (D)- or (L)-aspartic alc. that was incorporated into the interior of an ***antisense*** oligodeoxynucleotide. The stereocenter in the oligodeoxynucleotide interior originates from either (D)- or (L)-aspartic alc. The oligodeoxynucleotide portion of the oligodeoxynucleotide-peptide conjugate forms Watson-Crick base pairs with the single-stranded RNA that flanks the RNA hairpin loop. The pos. charged peptide makes specific electrostatic contacts with the neg. charged phosphate backbone of the RNA hairpin loop when attached to the N-allyl of (D)-aspartic alc. but does not have the proper orientation to make these electrostatic contacts when attached to the N-allyl of (L)-aspartic alc. This modeling study emphasizes the importance of stereocontrol at the point of branching in synthesizing oligodeoxynucleotide-peptide for binding of RNA hairpin loops.

L9 ANSWER 264 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:108346 CAPLUS
DN 124:282134
TI ***Antisense*** properties of duplex- and triplex-forming PNAs
AU Knudsen, Helle; Nielsen, Peter E.
CS Department Medical Biochemistry Genetics, Panum Institute, Copenhagen, DK-2200, Den.
SO Nucleic Acids Research (1996), 24(3), 494-500 CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB The potential of peptide nucleic acids (PNAs) as specific inhibitors of translation was studied. PNAs with a mixed purine/pyrimidine sequence form duplexes, whereas homopyrimidine PNAs form (***PNA***)2/RNA triplexes with complementary sequences on RNA. Neither of these ***PNA*** /RNA structures are substrates for RNase H. Translation expts. performed in cell-free exts. showed that a 15mer duplex-forming RNA blocked translation in a dose-dependent manner when the target was 5'-proximal to the AUG start codon on the RNA, whereas similar 10-, 15- or 20mer PNAs had no effect when targeted towards sequences in the coding region. Triplex-forming 10mer PNAs were efficient and specific ***antisense*** agents with a target overlapping the AUG start codon and caused arrest of ribosome elongation with a target positioned in the coding region of the mRNA. Furthermore, translation could be blocked with a 6mer bisPNA or with a clamp ***PNA*** , forming partly a triplex, partly a duplex, with its target sequence in the coding region of the mRNA.

L9 ANSWER 265 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:820572 CAPLUS
DN 123:228912
TI Preparation of nucleic acid-binding oligomers with amino acid-containing backbones and nucleobase-containing side chains.
IN Loebberding, Antonius; Mielkde, Burkhard; Schwemler, Christoph; Schwenner, Eckhardt; Stropp, Udo; Springer, Wolfgang; Kretschmer, Axel; Poetter, Thorsten
PA Bayer A.-G., Germany
SO Ger. Offen., 23 pp. CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI DE 4331012 A1 19950316 DE 1993-4331012 19930913 AU 9471543 A1 19950323 AU 1994-71543 19940829 AU 676349 B2 19970306 EP 646595 A1 19950405 EP 1994-113569 19940831 EP 646595 B1 19981104 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, SE AT 172984 E 19981115 AT 1994-113569 19940831 ES 2124345 T3 19990201 ES 1994-113569 19940831 US 5623049 A 19970422 US 1994-300884 19940906 JP 07118243 A2 19950509 JP 1994-239644 19940908 CA 2131755 AA 19950314 CA 1994-2131755 19940909
PRAI DE 1993-4331012 19930913

OS MARPAT 123:228912
AB Title compds. [I; A = (CH2)n, CO; B = (un)natural nucleoside base; D = (CO)p; E, G = CHR; R = H, (un)natural amino acid residue; E and G may be bonded to each other by (CH2)n; K = CO, SO2, CH2; M, L = H, carrier system, reporter ligand, solubilizing group; m = 0-3; n = 0-4; p, q = 0-2; s = 1-30], were prepd. Thus, H-(Q1)8-Ala-OH, prepd. by solid phase synthesis on phenylacetamidomethyl resin, showed concn.-dependent and sequence-selective binding to double-stranded DNA and showed stability to various proteases.

L9 ANSWER 266 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:816226 CAPLUS
DN 123:217580
TI Peptide nucleic acids as ***antisense*** therapeutic agents
AU Hanvey, Jeffery C.; Babiss, Lee E.
CS Department Cell Biology, GLAXO, Research Triangle Park, NC, USA
SO Delivery Strategies for Antisense Oligonucleotide Therapeutics (1995), 151-60. Editor(s): Akhtar, Saghir. Publisher: CRC, Boca Raton, Fla. CODEN: 61RXAX
DT Conference; General Review
LA English
AB A review with 14 refs. ***PNA*** (peptide-nucleic acids), their antigenic potential, and ***PNA*** cell-based studies are discussed.

L9 ANSWER 267 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:813051 CAPLUS
DN 123:190497
TI Preparation of dideoxynucleoside analogs and use of the analogs for DNA sequencing
IN Smith, Clifford; Fuller, Carl
PA Amersham International PLC, UK
SO PCT Int. Appl., 22 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9515395 A2 19950608 WO 1994-GB2630 19941201 WO 9515395 A3 19950727 W: CA, JP, US RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE CA 2174942 AA 19950608 CA 1994-2174942 19941201 EP 731846 A1 19960918 EP 1995-902208 19941201 EP 731846 B1 19990303 R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, NL, SE JP 09505736 T2 19970610 JP 1994-515489 19941201 AT 177151 E 19990315 AT 1995-902208 19941201 US 5702925 A 19971230 US 1996-649599 19960524
PRAI EP 1993-309597 19931201 WO 1994-GB2630 19941201
AB A method of making a dideoxynucleoside mono- or tri-phosphate, which is optionally 32-P or 33-P or 35-S radiolabeled, involved reacting the corresponding dideoxynucleoside with an optionally radiolabeled nucleotide phosphate or thiophosphate donor in the presence of a kinase or phosphotransferase enzyme which catalyzes the reaction. A method of sequencing nucleic acids by a chain termination technique involves detecting the products of enzymic synthesis by means of isotopically labeled chain terminating nucleotide analogs.

L9 ANSWER 268 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:795146 CAPLUS
DN 123:190496
TI Use of ***antisense*** oligomers in the control of contamination in nucleic acid amplification reactions
IN Ludtke, Douglas N.; Monahan, John E.; Unger, John T.
PA Ciba Corning Diagnostics Corp., USA
SO PCT Int. Appl., 49 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9514790 A1 19950601 WO 1994-IB366 19941121 W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG CA 2176805 AA 19950601 CA 1994-2176805 19941121 AU 9480664 A1 19950613 AU 1994-80664 19941121 AU 682226 B2 19970925 EP 726965 A1 19960821 EP 1994-931669 19941121 R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI JP 09505475 T2 19970603 JP 1994-514939 19941121 US 5763186 A 19980609 US 1997-778702 19970103
PRAI US 1993-157364 19931123 WO 1994-IB366 19941121
AB A novel process for the use of ***antisense*** oligonucleotides (clamp oligonucleotides) and their analogs to eliminate contamination in nucleic acid amplification reactions that require transcription, e.g. with Q.beta. replicase, is described. These oligonucleotides may prevent amplification (e.g. by disrupting secondary structures) or hydrolyze contaminant nucleic acids (e.g. ribozymes) after amplification. Oligonucleotide analogs, e.g. based on 2'-O-Me nucleotides, that form more stable hybrids than DNA or RNA oligonucleotides may be used to increase the effectiveness of the method.

L9 ANSWER 269 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:778900 CAPLUS
DN 123:191284
TI Peptide nucleic acids - a new group of DNA analogs
AU Zekanowski, Cezary
CS Zaklad Genetyki, Instytutu Matki i Dziecka, Warsaw, 01-211, Pol.
SO Postepy Biochemii (1995), 41(1), 32-8 CODEN: PSTBAH; ISSN: 0032-5422
PB Polskie Towarzystwo Biochemiczne
DT Journal; General Review
LA Polish
AB A review with 38 refs. on peptide nucleic acids, discussing their helix-forming properties, their potential as anti-gene and ***antisense*** therapeutic agents, and the possibility that there once was a " ***PNA*** world," preceding the present chem. system of proteins and nucleic acids.

L9 ANSWER 270 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:752363 CAPLUS
DN 124:9293
TI Solid support synthesis of a ***PNA*** -DNA hybrid
AU van der Laan, A. C.; Meeuwenoord, N. J.; Kuyl-Yeheskiely, E.; Oosting, R. S.; Brands, R.; van Boom, J. H.
CS Leiden Inst. Chem., Leiden Univ., Leiden, 2300 RA, Neth.
SO Recueil des Travaux Chimiques des Pays-Bas (1995), 114(6), 295-7 CODEN: RTCPA3; ISSN: 0165-0513
PB Elsevier
DT Journal
LA English
AB The solid support synthesis of a homothymine ***peptide*** ***nucleic*** ***acid*** (***PNA***)-DNA octamer (i.e. hybrid I; T = thymin-1-yl), which is an ***antisense*** oligonucleotide analog (no data), could be realized using tetrabutylammonium N-[2-(4- methoxytrityl)aminoethyl]-N-[(thymin-1-yl)acetyl]glycinate (II) as ***PNA*** building block and the resp. 2-cyanoethyl-N,N- diisopropylphosphoramidite derivs. of both 5'-O-(4,4'- dimethoxytrityl)thymidine and 5'-N-(4-

methoxytrityl)amino-5'- deoxythymidine (III; R = O-DMTr, NH-MMTr).

L9 ANSWER 271 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:732586 CAPLUS
DN 123:136022
TI Backbone modifications in oligonucleotides and ***peptide*** ***nucleic*** ***acid*** systems
AU De Mesmaeker, Alain; Altmann, Karl-Heinz; Waldner, Adrian; Wendeborn, Sebastian
CS Central Research Laboratories, Ciba-Geigy Ltd., Basel, CH-4002, Switz.
SO Current Opinion in Structural Biology (1995), 5(3), 343-55
CODEN: COSBEF; ISSN: 0959-440X
PB Current Biology
DT Journal; General Review
LA English
AB A review, with 92 refs. In the past year major advances have been made in the design, synthesis and characterization of two classes of modified oligonucleotides. In the first class, the phosphodiester backbone of 2'-deoxyribo-oligonucleotides has been replaced in several different ways. The second group represents a completely different type of oligonucleotide modification in which the backbone and the 2'-deoxyribose moieties are replaced by amino acids. These advances present new possibilities for the pharmaceutical application of modified oligonucleotides in ***antisense*** strategies.

L9 ANSWER 272 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:714603 CAPLUS
DN 123:122821
TI ***Antisense*** drug delivery through the blood-brain barrier
AU Boado, Ruben J.
CS Department of Medicine and Brain Research Institute, UCLA School of Medicine, Los Angeles, CA, 90095, USA
SO Advanced Drug Delivery Reviews (1995), 15(1-3), 73-107
CODEN: ADDREP; ISSN: 0169-409X
PB Elsevier
DT Journal; General Review
LA English
AB A review with 172 refs. The blood-brain barrier evolved to protect the brain against peripheral neurotransmitters, cytotoxins and microorganisms. This barrier prevents the delivery to brain of ***antisense*** oligomers and other potential therapeutics for the treatment of viral infections, tumors, and other brain disorders. The brain represents a shelter for the human immunodeficiency virus (HIV), for low grade gliomas, and early stages of metastatic tumors to the brain. Non-invasive delivery systems for ***antisense*** oligodeoxynucleotide (ODN) therapeutics have been developed that include transcellular avidin-based delivery systems, such as conjugates of avidin analogs and the monoclonal antibody directed to the transferrin receptor (OX26), which targets all tissues expressing these receptors including the blood-brain barrier and liver. This review discusses different approaches for delivery of ***antisense*** oligodeoxynucleotides to the brain and suggests that biotinylated ***PNA*** conjugated to avidin-based transcellular delivery system represents a model for the delivery of ***antisense*** therapeutics through the blood-brain barrier.

L9 ANSWER 273 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:713960 CAPLUS
DN 123:112638
TI Peptide nucleic acids containing nucleobases attached to serine/threonine by hemiaminal linkages for use as ***antisense*** probes and/or drug carriers
IN Garner, Philip P.
PA Case Western Reserve University, USA
SO PCT Int. Appl., 25 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9511909 A1 19950504 WO 1994-US11445 19941007 W: AU, CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE AU 9479724 A1 19950522 AU 1994-79724 19941007 US 5731416 A 19980324 US 1996-645930 19960514
PRAI US 1993-144705 19931028 WO 1994-US11445 19941007
OS MARPAT 123:112638
AB The present invention relates to the development of a new class of oligonucleotide surrogates capable of sequence specific binding to single-stranded DNA and RNA as well as to double-stranded DNA targets. More specifically, structures (Ser/Thr[CH2B]-AA[P])n (B=nucleobase such as A, C, G, T, and U; AA=.alpha.-amino acid; P=optional chem. probe; n>1) represent the repeating structural units for a no. of the nucleic acid surrogates of the present invention. Once synthesized (in suitably protected form), the monobasic units are linked together via peptide bonds to produce the required oligomeric structures having defined nucleobase sequences. These nucleic acid surrogates may then be utilized for use as ***antisense*** /antigene probes and/or drug carriers. The surrogates are derived from readily available .alpha.-amino acids and do not require asym. C-C bond formation. The nucleobases are attached to alternating Ser or Thr residues via a hemiaminal linkage which preserves the natural N-glycoside substructure. Chem. probes may be attached to the spacer amino acid, or alkylation of this residue may be useful for prevention of proteolysis. The synthesis of a repeating structural unit as well as a thymine-contg. tetrapeptide is presented.

L9 ANSWER 274 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:708426 CAPLUS
DN 123:74873
TI ***Peptide*** - ***nucleic*** ***acid*** oligomer inhibitors of human immunodeficiency virus replication
IN Ecker, David J.
PA Isis Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 185 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9504068 A1 19950209 WO 1994-US8517 19940728 W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG AU 9475164 A1 19950228 AU 1994-75164 19940728
PRAI US 1993-99718 19930729 WO 1994-US8517 19940728
AB A novel class of compds. known as peptide nucleic acids that bind complementary ssDNA and RNA strands more strongly than a corresponding DNA are used to develop ***antisense*** nucleic acids for control of the replication of human immunodeficiency virus. The peptide nucleic acids generally comprise ligands such as naturally occurring DNA bases attached to a peptide backbone through a suitable linker. The design and synthesis of oligonucleotides targetted against several genes of HIV-1 is demonstrated. PNAs directed against the tat gene of HIV-1 were shown to bind tat sequences in vitro.

L9 ANSWER 275 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1995:623532 CAPLUS
DN 123:5145
TI Biopolymer synthesis and analysis utilizing surface-activated organic polymers as solid support materials
IN Coassin, Peter J.; Matson, Robert S.; Rampal, Jang B.
PA Beckman Instruments, Inc., USA
SO PCT Int. Appl., 85 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9509176 A2 19950406 WO 1993-US9294 19930928 W: AU, CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE AU 9352944 A1 19950418 AU 1993-52944 19930928 AU 671688 B2 19960905 EP 721458 A1 19960717 EP 1993-923172 19930928 EP 721458 B1 20000517 R: DE, FR, GB
PRAI WO 1993-US9294 19930928
AB Surface-activated, org. polymers are used as solid support materials for biopolymer synthesis and anal. Most preferably, aminated polypropylene is used for the synthesis of oligonucleotides, and these devices are most preferably utilized for genetic anal. of patient samples. Wild-type target and mutation target oligonucleotides were synthesized directly to aminated polypropylene and these can be used for genetic screening; the ability to differentiate between the presence of wild-type complement and mutation is evident. The usage of aminated polypropylene is also illustrated by (1) the anal. of cystic fibrosis .DELTA.F508 exon 10, (2) anal. of hen egg lysozyme peptides, and (3) dipstick hybridization.

L9 ANSWER 276 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:622519 CAPLUS
DN 123:49929
TI DNA analogs with nonphosphodiester backbones
AU Nielsen, Peter E.
CS Cent. Biomol. Recognition, Univ. Copenhagen, Copenhagen, DK-2200, Den.
SO Annual Review of Biophysics and Biomolecular Structure (1995), 24, 167-83 CODEN: ABBSE4; ISSN: 1056-8700
PB Annual Reviews
DT Journal; General Review
LA English
AB This review with 74 refs. discusses the recent developments of DNA analogs with nonphosphodiester backbones in terms of DNA structure and ***antisense*** and antigene potential. A larger no. of derivs. are now available in which the phosphodiester linkage has been replaced but the deoxyribose retained. However, only a few of these (e.g. the ones having a thioformacetal or a carboxamide linkage) appear to be good structural DNA mimics. Two successful attempts to replace the entire deoxyribose phosphate backbone have been reported, the morpholino derivs. and the peptide nucleic acids (***PNA***), which contain an N-(2-aminoethyl)glycine-based pseudopeptide backbone. Most information is available on the ***PNA*** , which is a very promising DNA mimic. In conclusion, the deoxyribose phosphate backbone is not essential for a potent structural DNA mimic and not even required for a helical duplex structure.

L9 ANSWER 277 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:617334 CAPLUS
DN 123:131915
TI Vector-mediated delivery of a polyamide (" ***peptide*** ") ***nucleic*** ***acid*** analog through the blood-brain barrier in vivo
AU Pardridge, William M.; Boado, Ruben J.; Kang, Young-Sook
CS Dep. of Medicine and Brain Research Inst., Univ. of California, Los Angeles, CA, 90024, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1995), 92(12), 5592-6 CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Polyamide ("peptide") nucleic acids (PNAs) are mols. with antigene and ***antisense*** effects that may prove to be effective neuropharmaceuticals if these mols. are enabled to undergo transport through the brain capillary endothelial wall, which makes up the blood-brain barrier in vivo. The model ***PNA*** used in the present studies is an 18-mer that is ***antisense*** to the rev gene of human immunodeficiency virus type and is biotinylated at the amino terminus and iodinated at a tyrosine residue near the carboxyl terminus. The biotinylated ***PNA*** was linked to a conjugate of streptavidin (SA) and the OX26 murine monoclonal antibody to the rat transferrin receptor. The blood-brain barrier is endowed with high transferrin receptor concns., enabling the OX26-SA conjugate to deliver the biotinylated ***PNA*** to the brain. Although the brain uptake of the free ***PNA*** was negligible following i.v. administration, the brain uptake of the ***PNA*** was increased at least 28-fold when the ***PNA*** was bound to the OX26-SA vector. The brain uptake of the ***PNA*** bound to the OX26-SA vector was 0.1% of the injected dose per g of brain at 60 min after an i.v. injection, approximating the brain uptake of i.v. injected morphine. The ***PNA*** bound to the OX26-SA vector retained the ability to bind to synthetic rev mRNA as shown by RNase protection assay. In summary, the present studies show that while the transport of PNAs across the blood-brain barrier is negligible, delivery of these potential neuropharmaceutical drugs to the brain may be achieved by coupling them to vector-mediated peptide-drug delivery systems.

L9 ANSWER 278 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:603733 CAPLUS
DN 123:74896
TI ***Peptide*** - ***nucleic*** ***acid*** modulators of protein kinase C levels
IN Dean, Nicholas M.
PA ISIS Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 255 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9503833 A1 19950209 WO 1994-US8465 19940728 W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG AU 9475516 A1 19950228 AU 1994-75516 19940728
PRAI US 1993-99098 19930729 WO 1994-US8465 19940728
AB Peptide nucleic acids (PNAs) useful for regulating metabolic processes involving protein kinase C are described. These PNAs are ***antisense*** oligonucleotides directed against transcripts for specific isoenzymes of protein kinase C. These PNAs may be useful in the diagnosis and treatment of neoplastic, hyperproliferative and inflammatory disease amongst others. Design and synthesis of a no. of these PNAs is demonstrated.

L9 ANSWER 279 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:563178 CAPLUS

DN 123:189662
TI An assessment of the ***antisense*** properties of RNase H-competent and steric-blocking oligomers
AU Bonham, Michele A.; Brown, Stephen; Boyd, Ann L.; Brown, Pamela H.; Bruckenstein, David A.; Hanvey, Jeffery C.; Thomson, Stephen A.; Pipe, Adrian; Hassman, Fred; et al.
CS Dep. Mol. Cell Biol., Glaxo Res. Inst., Research Triangle Park, NC, 27709, USA
SO Nucleic Acids Research (1995), 23(7), 1197-203 CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB The ***antisense*** activity and gene specificity of two classes of oligonucleotides (ONs) were directly compared in a highly controlled assay. One class of ONs has been proposed to act by targeting the degrdn. of specific RNAs through an RNase H-mediated mechanism and consists of C-5 propynyl pyrimidine phosphorothioates ONs (propyne-S-ON). The second class of ***antisense*** agents has been proposed to function by sterically blocking target RNA formation, transport or translation and includes sugar modified (2'-O-allyl) ONs and peptide nucleic acids (PNAs). Using a CV-1 cell based microinjection assay, the authors targeted ***antisense*** agents representing both classes to various cloned sequences localized within the SV40 large T antigen RNA. The authors detd. the propyne-S-ON was the most potent and gene-specific agent of the two classes which likely reflected its ability to allow RNase H cleavage of its target. The ***PNA*** oligomer inhibited T Ag expression via an ***antisense*** mechanism, but was less effective than the propyne-S-ON; the lack of potency may have been due in part to the PNAs slow kinetics of RNA assocn. Interestingly, unlike the 2'-O-allyl ON, the ***antisense*** activity of the ***PNA*** was not restricted to the 5' untranslated region of the T Ag RNA. Based on these findings the authors conclude that PNAs could be effective ***antisense*** agents with addnl. chem. modification that will lead to more rapid assocn. with their RNA target.

L9 ANSWER 280 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:412171 CAPLUS
DN 123:217925
TI Impact of biophysical parameters on the biological assessment of peptide nucleic acids, ***antisense*** inhibitors of gene expression
AU Noble, Stewart A.; Bonham, Michele A.; Bisi, John E.; Bruckenstein, David A.; Brown, Pamela H.; Brown, Stephen C.; Cadilla, Rodolfo; Gaul, Micheal D.; Hanvey, Jeffrey C.; et al.
CS Depts. Med. Chem., Glaxo Res. Inst., Greenford, UK
SO Drug Development Research (1995), 34(2), 184-95 CODEN: DDREDK; ISSN: 0272-4391
PB Wiley-Liss
DT Journal
LA English
AB Peptide nucleic acids (***PNA***) are oligodeoxynucleotide (ODN) analogs in which the sugar phosphate backbone of the ODN has been replaced by one derived from units of N-ethylaminoglycine. PNAs recognize DNA and RNA in a sequence specific manner and form complexes that can be characterized by biophys. methods. The binding motif is context dependent; homopyrimidine PNAs combine with complementary polypurine targets to form stoichiometric 2:1 complexes, whereas PNAs contg. both purine and pyrimidine bases afford a 1:1 heteroduplex with mis-match sensitivity comparable to that found in dsDNA. These complexes mediate the antigene and ***antisense*** effects of PNAs via the steric blockade of enzyme complexes responsible for DNA transcription, cDNA synthesis, and RNA translation. PNAs, like ODNs, are taken up by cells via endocytosis leading to their entrapment within intracytoplasmic vesicles. Under circumstances where agent delivery is solved by cell microinjection, PNAs can effect selective inhibition of endogenous and exogenous genes. The impact of biophys. parameters on the biol. assessment of PNAs as ***antisense*** inhibitors of gene expression is presented and discussed.

L9 ANSWER 281 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:362885 CAPLUS
DN 122:214508
TI Positive-ion fast-atom bombardment tandem mass spectrometry of peptide nucleic acids
AU Takao, Toshifumi; Fukuda, Hiroyuki; Coull, James; Shimonishi, Yasutsugu
CS Inst. Protein Res., Osaka Univ., Osaka, 565, Japan
SO Rapid Communications in Mass Spectrometry (1994), 8(12), 925-8 CODEN: RCMSEF; ISSN: 0951-4198
PB Wiley
DT Journal
LA English
AB The base sequence of synthetic peptide nucleic acids (PNAs), novel ***antisense*** agents, was analyzed by pos.-ion fast-atom bombardment tandem mass spectrometry (FAB-MS/MS). Upon high-energy collisional activation decompn., ***PNA*** oligomers provided apparent MS/MS product ions resulting from specific cleavage along the ***PNA*** backbone.

L9 ANSWER 282 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:238169 CAPLUS
DN 122:38716
TI Interaction between charged peptides and nucleic acids: development of a histone- or peptide-mediated potential drug delivery system
AU Wada, Akira; Suzuki, Yosuke; Okayama, Minenobu; Sato, Shuji; Shimayama, Takashi; Oya, Masanao; Uchida, Chieko; Koguma, Tetsuhiko; Nishikawa, Satoshi; et al.
CS National Inst. Biosci. Human Technology, AIST, 305, Japan
SO Nucleic Acids Symposium Series (1994), 31(21st Symposium on Nucleic Acids Chemistry, 1994), 227-8 CODEN: NACSD8; ISSN: 0261-3166
PB Oxford University Press
DT Journal
LA English
AB As a step toward the goal to develop a highly efficient nucleic acid delivery system, that might facilitate receptor-mediated endocytosis of DNA/RNA macromols. into cells, we examd. interactions between pos. charged polypeptides and neg. charged nucleic acids. Poly-cationic amino acids used in this study included poly-L-Lysine, poly-L-(Lysine:Serine) random copolymer, poly(D,L)-Lysine random copolymer, and histone. Ribozymes and ***antisense*** oligonucleotides, that are thought to be interesting tools for selective inhibition of gene expression, were found to form complexes with poly-cationic amino acids except the poly(D,L)-Lysine random copolymer. Such complexes were much more resistant to degrdn. by nucleases in human serum. Com. available histone may be used as a carrier for ***antisense*** DNA and plasmids. However, it was not a suitable carrier for ribozymes or ***antisense*** RNA because it was contaminated with significant amt. of RNases. Available data suggest that oligonucleotide:poly-cationic amino acid complexes have high potential as carriers for oligonucleotide drugs.

L9 ANSWER 283 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:708297 CAPLUS
DN 121:308297

TI Anthrax toxin fusion proteins for use in the targetting of cytotoxic activity
IN Leppla, Stephen H.; Klimpel, Kurt; Arora, Naveen; Singh, Yogendra; Nichols, Peter J.
PA United States Dept. of Health and Human Services, USA
SO PCT Int. Appl., 123 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9418332 A2 19940818 WO 1994-US1624 19940214 WO 9418332 A3 19941013 W: AU, CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE US 5591631 A 19970107 US 1993-21601 19930212 US 5677274 A 19971014 US 1993-82849 19930625 AU 9463922 A1 19940829 AU 1994-63922 19940214 AU 682500 B2 19971009 EP 684997 A1 19951206 EP 1994-911385 19940214 EP 684997 B1 19980819 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
PRAI US 1993-21601 A 19930212 US 1993-82849 A 19930625 WO 1994-US1624 W 19940214
AB Chimeric genes for fusion proteins of anthrax protective antigen (PA), the binding domain of the native anthrax lethal factor (LF) protein and an activity inducing domain of a second protein are described for manuf. of the protein for targetted delivery of the biol. active protein domain. The second domain may be a toxin or an endogenous regulator of growth or function. Chimeric genes for fusion proteins of a translocation domain and LF binding domain of the native anthrax PA protein and a ligand domain that specifically binds a cellular target are also described. The anthrax protective antigen may be an analog in which the trypsin cleavage site is replaced with one recognized specifically by the HIV-1 proteinase. A series of genes for fusion proteins of LF and Pseudomonas exotoxins were constructed and expressed in Escherichia coli and tested for cytotoxic activity against CHO cells. All of the fusio proteins tested were cytotoxic with the relationship between activity and the domains of the LF indicated that domain III was the active domain with domain II inhibiting this activity. A sequence (amino acids 251-278) of the Pseudomonas exotoxin appeared to act as a stop transfer peptide. The prepn. of fusion products with single-chain antibodies is described.

L9 ANSWER 284 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:621881 CAPLUS
DN 121:221881
TI NMR solution structure of a ***peptide*** ***nucleic*** ***acid*** complexed with RNA
AU Brown, Stephen C.; Thomson, Stephen A.; Veal, James M.; Davis, Donald G.
CS Glaxo Res. Inst., Res. Triangle Park, NC, 27709, USA
SO Science (Washington, DC, United States) (1994), 265(5173), 777-7 CODEN: SCIEAS; ISSN: 0036-8075
DT Journal
LA English
AB Peptide nucleic acids (***PNA***) incorporating nucleic acid bases into an achiral polyamide backbone bind to DNA in a sequence-dependent manner. The structure of a ***PNA*** -RNA complex was detd. with NMR methods. A hexameric ***PNA*** formed a 1:1 complex with a complementary RNA that is an antiparallel, right-handed double helix with Watson-Crick base pairing similar to the "A" form structure of RNA duplexes. The achiral ***PNA*** backbone assumed a distinct conformation upon binding that differed from previously proposed models and provides a basis for further structure-based design of ***antisense*** agents.

L9 ANSWER 285 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:570492 CAPLUS
DN 121:170492
TI Sequence selective recognition of DNA by ***peptide*** ***nucleic*** ***acid*** (***PNA***)
AU Nielsen, Peter E.
CS Panum Institute, University Copenhagen, Copenhagen, DK 2200, Den.
SO Struct. Biol. State of the Art, Proc. Conversation Discip. Biomol. Stereodyn., 8th (1994), Meeting Date 1993, Volume 1, 247-50. Editor(s): Sarma, Ramaswamy H.; Sarma, Mukti H. Publisher: Adenine, Schenectady, N. Y. CODEN: 60GVAZ
DT Conference
LA English
AB ***PNA*** (***peptide*** ***nucleic*** ***acid***) is a structural DNA mimic with an N-(2-aminoethyl)glycine backbone, ***PNA*** forms stable duplexes with Watson-Crick complementary oligonucleotides, and homo-pyrimidine ***PNA*** binds to complementary targets in duplex DNA by strand displacement. Model expts. support the potential of ***PNA*** as ***anti*** - ***sense*** or anti-gene gene-targeted drugs and as biomol. tools.

L9 ANSWER 286 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:127922 CAPLUS
DN 120:127922
TI ***Peptide*** ***nucleic*** ***acid*** (***PNA***) conformation and polymorphism in ***PNA*** -DNA and ***PNA*** -RNA hybrids
AU Almarsson, Orn; Bruice, Thomas C.
CS Dep. Chem., Univ. California, Santa Barbara, CA, 93106, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1993), 90(20), 9542-6 CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB Two hydrogen-bonding motifs have been proposed to account for the extraordinary stability of polyamide " ***peptide*** " ***nucleic*** ***acid*** (***PNA***) hybrids with nucleic acids. These interresidue- and intraresidue-hydrogen-bond motifs were investigated by mol. mechanics calcns. Energy-minimized structures of Watson-Crick base-paired decameric duplexes of ***PNA*** with A-, B-, and Z-DNA and A-RNA polymorphs indicate that the inherent stability of the complementary ***PNA*** helical structures is derived from interresidue, rather than from intraresidue, hydrogen bonds in all hybrids studies. Intraresidue-hydrogen-bond lengths are consistently longer than interresidue hydrogen bonds. Helical strand stability with interresidue hydrogen bond stabilization follows the order: B-(DNA.cntdot. ***PNA***) > A-(DNA.cntdot. ***PNA***) .simeq. A-RNA.cntdot. ***PNA*** > Z-(DNA.cntdot. ***PNA***). In the triplex hybrids A-(RNA.cntdot.PNA2) and B-(DNA.cntdot.PNA2), differences between stabilities of the two decamers of thyminyl ***PNA*** with lysine amide attached to the C terminus (pnaT)10 strands are small. The Hoogsteen (pnaT)10 strands are of slightly higher potential energy than are the Watson-Crick (pnaT)10 strands. Antiparallel arrangement of PNAs in the triplex is slightly favored over the parallel arrangement based on the calcns. Examn. by mol. mechanics of the ***PNA*** .cntdot.DNA analog of the NMR-derived structure for the B-double-stranded DNA dodecamer d(CGCAAATTTGCG)2 in soln. suggests that use of all bases of the genetic alphabet should be possible without loss of the specific interresidue-hydrogen-bonding pattern within the ***PNA*** strand.

L9 ANSWER 287 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:124252 CAPLUS
DN 120:124252

TI Characterization of ***antisense*** binding properties of peptide nucleic acids by capillary gel electrophoresis
AU Rose, Donald J.
CS Bioanal. Struct. Chem. Dep., Glaxo Res. Inst., Research Triangle Park, NC, 27709, USA
SO Analytical Chemistry (1993), 65(24), 3545-9 CODEN: ANCHAM; ISSN: 0003-2700
DT Journal
LA English
AB The binding of peptide nucleic acids (PNAs), novel ***antisense*** agents, to their complementary oligonucleotide is characterized by capillary gel electrophoresis (CGE). The ability of CGE to resolve the free and bound species enables the measurement of relative binding kinetics and the stoichiometry of binding. The binding kinetics depend on the relative sequence orientation of the target oligonucleotides. The stoichiometry of binding is 1:1 for the ***PNA*** -oligodeoxynucleotide heteroduplex whereas the stoichiometry for the ***PNA*** - oligoribonucleotide is more complicated.

L9 ANSWER 288 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:99667 CAPLUS
DN 120:99667
TI Strand-invasion of duplex DNA by ***peptide*** ***nucleic*** ***acid*** oligomers
AU Peffer, Nancy J.; Hanvey, Jeffery C.; Bisi, John E.; Thomson, Stephen A.; Hassman, C. Fred; Noble, Stewart A.; Babiss, Lee E.
CS Res. Inst., Glaxo, Inc., Research Triangle Park, NC, 27709, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1993), 90(22), 10648-52 CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB Polyamide oligomers, termed peptide nucleic acids (PNAs), bind with high affinity to both DNA and RNA and offer both ***antisense*** and antigene approaches for regulating gene expression. When a ***PNA*** binds to a complementary sequence in a double-stranded DNA, one strand of the duplex is displaced, and a stable D-loop is formed. Unlike oligodeoxynucleotides for which binding polarity is detd. by the deoxyribose sugar, the unrestrained polyamide backbone of the ***PNA*** could permit binding to a DNA target in an orientation independent manner. The authors now provide evidence that PNAs can, in fact, bind to their complementary sequence in DNA independent of the DNA-strand polarity - i.e., a ***PNA*** binds to DNA in both "parallel" and "antiparallel" fashion. With a mixed-sequence 15-mer ***PNA*** , kinetic studies of ***PNA*** .cntdot.DNA interactions revealed that D-loop formation was rapid and the complex was stable for several hours. However, when measured either by gel-mobility-shift anal. or RNA polymerase II-elongation termination, D-loop formation was salt dependent, but ***PNA*** -strand dissocn. was not salt dependent. The authors obsd. that D-loop-contg. DNA fragments had anomalous gel mobilities that varied as a function of the position of the D-loop relative to the DNA termini. On the basis of permutation anal., the decreased mobility of the ***PNA*** .cntdot.DNA complex was attributed to a bend in the DNA at or near the D-loop.

L9 ANSWER 289 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:531031 CAPLUS
DN 119:131031
TI Peptide nucleic acids (PNAs): Potential ***antisense*** and anti-gene agents
AU Nielsen, Peter E.; Egholm, Michael; Berg, Rolf H.; Buchardt, Ole
CS Dep. Biochem. B, Panum Inst., Copenhagen, DK-2200, Den.
SO Anti-Cancer Drug Design (1993), 8(1), 53-63 CODEN: ACDDEA; ISSN: 0266-9536
DT Journal
LA English
AB The binding of peptide nucleic acids (PNAs) T10-LysNH2, T5CT4-LysNH2 and T2CT2CT4-LysNH2 to double-stranded DNA targets A10, A5GA4 and A2GA2GA4 was studied by nuclease S1 probing. It is found that the PNAs bind preferentially to their complementary targets, weaker to targets contg. one mismatch and not to targets contg. two mismatches. Using an RNA polymerase T3 in vitro transcription system, it is found that a ***PNA*** T10-LysNH2 bound downstream from the promoter causes transcription elongation arrest at the ***PNA*** binding site only when the ***PNA*** is bound to the template strand. Finally, it is shown that primer extension by Taq DNA polymerase on a single-stranded template is arrested at an occupied ***PNA*** T10 binding site. These results are discussed in relation to PNAs as potential ***anti*** - ***sense*** and anti-gene drugs.

L9 ANSWER 290 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:226662 CAPLUS
DN 118:226662
TI ***Antisense*** and antigen properties of peptide nucleic acids
AU Hanvey, Jeffery C.; Peffer, Nancy J.; Bisi, John E.; Thomson, Stephen A.; Cadilla, Rodolfo; Josey, John A.; Ricca, Daniel J.; Hassman, C. Fred; Bonham, Michele A.; et al.
CS Dep. Cell Biol., Glaxo Inc., Research Triangle Park, NC, 27709, USA
SO Science (Washington, DC, United States) (1992), 258(5087), 1481-5 CODEN: SCIEAS; ISSN: 0036-8075
DT Journal
LA English
AB Peptide nucleic acids (PNAs) are polyamide oligomers that can strand invade duplex DNA, causing displacement of one DNA strand and formation of a D-loop. Binding of either a T10 ***PNA*** (T stands for thymidine) or a mixed sequence 15-mer ***PNA*** to the transcribed strand of a G-free transcription cassette caused 90 to 100 percent site-specific termination of RNA polymerase (pol) II transcription elongation. When a T10 ***PNA*** was bound on the nontranscribed strand, site-specific inhibition never exceeded 50 percent. Binding of PNAs to RNA resulted in site-specific termination of both reverse transcription and in vitro translation, precisely at the position of the ***PNA*** .RNA heteroduplex. Nuclear microinjection of cells constitutively expressing SV40 large T antigen (T Ag) with either a 15-mer or 20-mer ***PNA*** targeted to the T Ag mRNA suppressed T Ag expression. This effect was specific in that there was no redn. in .beta.-galactosidase expression from a coinjected expression vector and no inhibition of T Ag expression after microinjection of a 10-mer ***PNA*** .

L9 ANSWER 291 OF 291 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:116074 CAPLUS
DN 118:116074
TI New ***antisense*** nucleic acids. Peptide nucleic acids (***PNA***) with strong DNA binding activities
AU Sekine, Mitsuo
CS Fac. Biosci. Biotechnol., Tokyo Inst. Technol., Yokohama, 227, Japan
SO Kagaku (Kyoto, Japan) (1993), 48(1), 64 CODEN: KAKYAU; ISSN: 0451-1964
DT Journal; General Review
LA Japanese

AB A review with 5 refs. on ***PNA*** with a N-(2-amonoethyl)glycine backbone prepd. by solid phase synthesis using pentafluorophenylester type active esters. ***PNA*** shows high m.p.s in hybridization with DNA and lacks chirality. ***PNA*** is expected to be useful in gene therapy.

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